

10/750,743

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1204bxd

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 "Ask CAS" for self-help around the clock  
NEWS 3 SEP 01 INPADOC: New family current-awareness alert (SDI) available  
NEWS 4 SEP 01 New pricing for the Save Answers for SciFinder Wizard within  
STN Express with Discover!  
NEWS 5 SEP 01 New display format, HITSTR, available in WPIDS/WPINDEX/WPIX  
NEWS 6 SEP 27 STANDARDS will no longer be available on STN  
NEWS 7 SEP 27 SWETSCAN will no longer be available on STN  
NEWS 8 OCT 28 KOREAPAT now available on STN  
NEWS 9 NOV 18 Current-awareness alerts, saved answer sets, and current  
search transcripts to be affected by CERAB, COMPUAB, ELCOM,  
and SOLIDSTATE reloads  
NEWS 10 NOV 30 PHAR reloaded with additional data  
NEWS 11 DEC 01 LISA now available on STN  
  
NEWS EXPRESS OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS INTER General Internet Information  
NEWS LOGIN Welcome Banner and News Items  
NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that  
specific topic.

All use of STN is subject to the provisions of the STN Customer  
agreement. Please note that this agreement limits use to scientific  
research. Use for software development or design or implementation  
of commercial gateways or other similar uses is prohibited and may  
result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 17:50:50 ON 06 DEC 2004

=> fil reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 17:50:54 ON 06 DEC 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 5 DEC 2004 HIGHEST RN 792236-36-3  
DICTIONARY FILE UPDATES: 5 DEC 2004 HIGHEST RN 792236-36-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

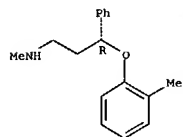
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> s atomoxetine/cn  
L1 1 ATOMOXETINE/CN

=> d l1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 83015-26-3 REGISTRY  
 CN Benzenepropanamine, N-methyl-γ-(2-methylphenoxy)-, (γR)- (9CI)  
 (CA INDEX NAMES)  
 OTHER CA INDEX NAMES:  
 CN Benzenepropanamine, N-methyl-γ-(2-methylphenoxy)-, (R)-  
 OTHER NAMES:  
 CN (-)-Tomoxetine  
 CN Atomoxetine  
 CN Tomoxetine  
 FS STEREOSEARCH  
 MF C17 H21 N O  
 CI COM  
 LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN\*, BIOBUSINESS,  
 BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBND, CHEMCATS, CHEMINFORMRX,  
 CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA,  
 MEDLINE, MRCK\*, PHAR, PROMT, PROUSDDR, SYNTHLINE, TOXCENTER, USAN,  
 USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: WHO  
 DT.CA Caplus document type: Conference; Journal; Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC  
 (Process); RACT (Reactant or reagent); USES (Uses)  
 RLD.P Roles for non-specific derivatives from patents: BIOL (Biological  
 study); USES (Uses)  
 RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological  
 study); PREP (Preparation); PROC (Process); PRP (Properties); USES  
 (Uses)  
 RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological  
 study)

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

109 REFERENCES IN FILE CA (1907 TO DATE)  
 3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 109 REFERENCES IN FILE CAPLUS (1907 TO DATE)

|                      |            |         |
|----------------------|------------|---------|
| => fil caplus        |            |         |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL   |
|                      | ENTRY      | SESSION |
| FULL ESTIMATED COST  | 7.46       | 7.67    |

FILE 'CAPLUS' ENTERED AT 17:52:29 ON 06 DEC 2004  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
 COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 6 Dec 2004 VOL 141 ISS 24  
 FILE LAST UPDATED: 5 Dec 2004 (20041205/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s atomox?
L2      50 ATOMOX?

=> s atomoxetine
L3      50 ATOMOXETINE

=> s 83015-26-3/rn
      109 83015-26-3
      3 83015-26-3D
L4      107 83015-26-3/RN
      (83015-26-3 (NOTL) 83015-26-3D )

=> s 83015-26-3D/rn
L5      3 83015-26-3D/RN
      (83015-26-3D)

=> s l4 or l5
L6      109 L4 OR L5

=> s sex?
L7      143300 SEX?

=> s l6 and l7
L8      3 L6 AND L7

=> d l8 1-3 abs ibib hitstr
```

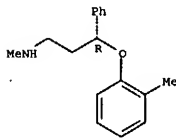


L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A review. Atomoxetine is the first nonstimulant drug approved by the United States Food and Drug Administration (FDA) for the treatment of attention-deficit-hyperactivity disorder (ADHD), and the only agent approved by the FDA for the treatment of ADHD in adults. Atomoxetine is a norepinephrine transport inhibitor that acts almost exclusively on the noradrenergic pathway. Its mechanism of action in the control and maintenance of ADHD symptoms is thought to be through the highly specific presynaptic inhibition of norepinephrine. Clin. trials to evaluate the short-term effects of atomoxetine in children and adults have shown that atomoxetine is effective in maintaining control of ADHD. Likewise, long-term trials have determined that atomoxetine is effective in preventing relapse of ADHD symptoms without an increase in adverse effects. A comparative trial of atomoxetine with methylphenidate in school-aged children indicated similar safety and efficacy without the abuse liability associated with some psychostimulants. The most commonly reported adverse effects in children and adolescents are dyspepsia, nausea, vomiting, decreased appetite, and weight loss. The rates of adverse events in the trials were similar for both the once- and twice-daily dosing regimens. The discontinuation rate was 3.5% in patients treated with atomoxetine vs. 1.4% for placebo and appeared to be dose dependent, with a higher percentage of discontinuation at dosages greater than 1.5 mg/kg/day. In clin. trials involving adults, the emergence of clin. significant or intolerable adverse events was low. The most common adverse events in adults were dry mouth, insomnia, nausea, decreased appetite, constipation, urinary retention or difficulties with micturition, erectile disturbance, dysmenorrhea, dizziness, and decreased libido. **Sexual** dysfunction occurred in approx. 2% of patients treated with atomoxetine. Atomoxetine should be used with caution in patients who have hypertension or any significant cardiovascular disorder. Overall, atomoxetine therapy in patients with ADHD appears to be effective in controlling symptoms and maintaining remission, with the advantages being comparable efficacy with that of methylphenidate, a favorable safety profile, and non-controlled substance status. Addnl. long-term studies are needed to determine its continued efficacy for those who require lifelong treatment, and comparative trials against other stimulant and nonstimulant agents.

ACCESSION NUMBER: 2004:719696 CAPLUS  
 DOCUMENT NUMBER: 141:306872  
 TITLE: Atomoxetine, a novel treatment for attention-deficit-hyperactivity disorder  
 AUTHOR(S): Christman, Alisa K.; Fermo, Joli D.; Markowitz, John S.  
 CORPORATE SOURCE: Departments of Pharmacy Practice, Medical University of South Carolina, Charleston, USA  
 SOURCE: Pharmacotherapy (2004), 24(8), 1020-1036  
 CODEN: PHPTDQ; ISSN: 0277-0008  
 PUBLISHER: Pharmacotherapy Publications  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English  
 IT 83015-26-3, Atomoxetine  
 RL: ADV (Adverse effect, including toxicity); DNA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (atomoxetine for attention-deficit-hyperactivity disorder)

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RN 83015-26-3 CAPLUS  
 CN Benzenepropanamine, N-methyl-γ-(2-methylphenoxy)-, (γR)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



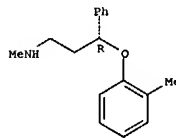
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Background and Objectives: Atomoxetine is a treatment for attention-deficit/hyperactivity disorder and is primarily eliminated via cytochrome P 4502D6 (CYP2D6). The pharmacokinetics of atomoxetine and its primary metabolites were investigated in 10 adults with hepatic impairment (6 moderate, 4 severe) and 10 age- and sex-matched control subjects, all being genotyped as CYP2D6 extensive metabolizers. Methods: A single oral 20-mg dose of atomoxetine was given. Multiple blood samples were collected for 48 h in healthy subjects and for 120 h in patients. Urine was collected up to 24 h. Before atomoxetine administration (10-20 days), sorbitol clearance and debrisoquin (INN, debrisoquine) metabolic ratio were determined as markers of hepatic blood flow and CYP2D6 activity, resp. Results: The systemic clearance of atomoxetine was significantly reduced in those with hepatic impairment compared with controls, thereby resulting in increased exposure (area under the concentration-time curve from time 0 to infinity, 1.58 vs. 0.85 μg · h<sup>-1</sup> · mL<sup>-1</sup>; P =.035) but no change in maximum concentration. Mean 4-hydroxyatomoxetine area under the concentration-time curve from time 0 to time t and maximum concentration were increased approx. 7-fold and 2-fold, resp. (P =.0001 and P =.0056, resp.). For the glucuronide conjugate of 4-hydroxyatomoxetine, the mean half-life was longer and the mean area under the concentration-time curve from time 0 to infinity and the maximum concentration were lower (P =.0028, P =.003, and P =.0001, resp.). The sorbitol clearance was lower and the debrisoquin metabolic ratio was higher, reflecting reduced hepatic blood flow and decreased CYP2D6 activity, resp. Decreased atomoxetine clearance in patients with hepatic impairment was clearly correlated with decreased CYP2D6 activity and decreased hepatic blood flow. Mean atomoxetine plasma protein binding was lower in patients with hepatic impairment compared with controls (96.5% vs. 98.7%, P =.0008). Atomoxetine was well tolerated in the 2 populations. Conclusion: For patients with attention-deficit/hyperactivity disorder who have hepatic impairment, dosage adjustment is recommended. Initial target doses should be reduced to 25% and 50% of the normal dose for patients with severe and moderate hepatic impairment, resp.

ACCESSION NUMBER: 2003:212349 CAPLUS  
 DOCUMENT NUMBER: 139:316551  
 TITLE: Effect of hepatic impairment on the pharmacokinetics of atomoxetine and its metabolites  
 AUTHOR(S): Chalon, Stephan A.; Desager, Jean-Pierre; DeSante, Karl A.; Frye, Reginald F.; Witcher, Jennifer; Long, Amanda J.; Sauer, John-Michael; Golner, Jean-Luc; Smith, Brian P.; Thomasson, Holly R.; Horrmann, Yves  
 CORPORATE SOURCE: Lilly Res. Lab., Indianapolis, IN, USA  
 SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (2003), 73(3), 178-191  
 CODEN: CLPTAT; ISSN: 0009-9236  
 PUBLISHER: Mosby, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 83015-26-3, Atomoxetine

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 RL: PKT (Pharmacokinetics); BIOL (Biological study)  
 (effect of hepatic impairment on pharmacokinetics of atomoxetine and its metabolites in relation to CYP2D6 genotype)  
 RN 83015-26-3 CAPLUS  
 CN Benzenepropanamine, N-methyl-γ-(2-methylphenoxy)-, (γR)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

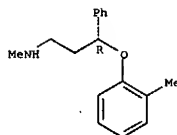
L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN  
AB A composition comprising: (a) a pharmaceutically effective amount of one or more norepinephrine reuptake inhibitors or a salt; and (b) 1 or more neuroleptics is provided. The composition is useful in treating disorders of diseases of the central nervous system, and particularly useful in treating schizophrenia. A pharmaceutical composition was prepared by combining reboxetine with a neuroleptic in an acceptable carrier. The composition contains 0.01-10 mg reboxetine and 25-300 mg clozapine.  
ACCESSION NUMBER: 2002:521465 CAPLUS  
DOCUMENT NUMBER: 137:98994  
TITLE: Pharmaceuticals containing a combination of norepinephrine reuptake inhibitors and neuroleptics  
INVENTOR(S): Wong, Erik Ho Fong; Gallen, Christopher C.; Svensson, Torgny  
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA; Pharmacia AB  
SOURCE: PCT Int. Appl., 22 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO. | DATE       |
|------------------------|--|----------|-----------------|------------|
| WO 2002053140          | A2   | 20020711 | WO 2001-US45871 | 20011227   |
| WO 2002053140          | A3   | 20021024 |                 |            |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |            |
| RW:                    | GH, CM, KE, LS, MW, MZ, SD, SI, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |            |
| CA 2431041             | AA   | 20020711 | CA 2001-2431041 | 20011227   |
| EP 1353675             | A2   | 20031022 | EP 2001-991997  | 20011227   |
| R:                     | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |          |                 |            |
| JP 2004517112          | T2   | 20040610 | JP 2002-554091  | 20011227   |
| US 2002156067          | A1   | 20021024 | US 2001-35100   | 20011228   |
| PRIORITY APPLN. INFO.: |  |          | US 2001-259286P | P 20010102 |
|                        |  |          | WO 2001-US45871 | W 20011227 |

IT 83015-26-3, Tomoxetine  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceuticals containing combination of norepinephrine reuptake inhibitors and neuroleptics)  
RN 83015-26-3 CAPLUS  
CN Benzenepropanamine, N-methyl-γ-(2-methylphenoxy)-, (γR)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



=> d his

(FILE 'HOME' ENTERED AT 17:50:50 ON 06 DEC 2004)

FILE 'REGISTRY' ENTERED AT 17:50:54 ON 06 DEC 2004

L1 1 S ATOMOXETINE/CN

FILE 'CAPLUS' ENTERED AT 17:52:29 ON 06 DEC 2004

L2 50 S ATOMOX?

L3 50 S ATOMOXETINE

L4 107 S 83015-26-3/RN

L5 3 S 83015-26-3D/RN

L6 109 S L4 OR L5

L7 143300 S SEX?

L8 3 S L6 AND L7

=> s 16 not 18

L9 106 L6 NOT L8

=> d 19 1-106 abs ibib

L9 ANSWER 1 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The invention relates to a method of treating at least one symptom of a lower urinary tract disorder in a subject in need of treatment wherein the symptom is selected from the group consisting of urinary frequency, urinary urgency, urinary urge incontinence, nocturia and enuresis. The method comprises administering to a subject in need of treatment a therapeutically effective amount of a compound that has 5-HT<sub>3</sub> receptor antagonist activity and NorAdrenaline Reuptake Inhibitor (NARI) activity. The invention further relates to a method of treating at least one symptom of a lower urinary tract disorder in a subject in need of treatment wherein the symptom is selected from the group consisting of urinary frequency, urinary urgency, urinary urge incontinence, nocturia and enuresis, comprising coadministering to said subject a first amount of a 5HT<sub>3</sub> antagonist and a second amount of a NARI, wherein the first and second amounts together comprise a therapeutically effective amount or are each present in a therapeutically effective amount. Administration of MCI-225 to rat or cat models of overactive bladder caused a significant dose-dependent increase in bladder capacity.

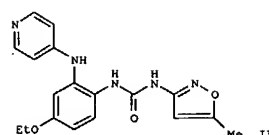
ACCESSION NUMBER: 2004:878266 CAPLUS  
 DOCUMENT NUMBER: 141:343543  
 TITLE: Method of treating lower urinary tract disorders with 5-HT<sub>3</sub> receptor antagonist and noradrenaline reuptake inhibitor combination  
 INVENTOR(S): Landau, Steven B.; Miller, Cheryl L.; Fraser, Matthew O.  
 PATENT ASSIGNEE(S): Dynogen Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 104 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2004089288   | A2   | 20041021 | WO 2004-US10088 | 20040402   |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |            |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SI, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| US 2004209869   | A1   | 20041021 | US 2004-817332  | 20040402   |
| PRIORITY APPLN. INFO.:  |      |          | US 2003-461022P | P 20030404 |
|   |      |          | US 2003-496502P | P 20030820 |
|   |      |          | US 2004-536341P | P 20040113 |

L9 ANSWER 2 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2004085433   | A2   | 20041007 | WO 2004-IB838   | 20040315   |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |            |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SI, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| PRIORITY APPLN. INFO.:  |      |          | US 2003-458766P | P 20030328 |

L9 ANSWER 2 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB The invention provides di(hetero)aryleureas A-NH-C(=X)-NH-B (I; X = O or S; A = certain (un)substituted 6-membered (hetero)aryl rings containing 0-4 N atoms, e.g., Ph, pyridinyl; B = certain (un)substituted 5- or 6-membered (hetero)aromatic rings containing 0, NH or derivs., N, or S, particularly 6-membered rings with 0-4 N as cited of A, or 5-membered azole-type heterocycles bound at C or N). These compds. may be in the form of pharmaceutical salts or compns., or may be in pure enantiomeric form or racemic mixts. I are useful in pharmaceuticals used to treat a wide variety of diseases or conditions in which the α7 subunit of the nicotinic acetylcholine receptor (α7nAChR) is known to be involved. I may be used in combination with a variety of other agents, including antipsychotics, agents which increase brain acetylcholine levels, or which inhibit acetylcholinesterase, or which activate production of acetylcholine, or monoamine reuptake inhibitors, psychostimulants, or α7nAChR agonists. A total of 25 compds. are described, 23 with preparatory details. Using a FLIPR, cell-based, Ca flux assay with mutated α7nAChR expressed in SHEP-1 cells, the example compds. had activity between 10 nM and 10 μM. For instance, invention compound II was prepared in 4 steps. Thus, ethanolysis of 2-bromo-4-fluoro-1-nitrobenzene with NaOEt in EtOH (68%), and Pd complex-catalyzed coupling of the resultant N-(5-ethoxy-2-nitrophenyl)pyridin-4-amine. Hydrogenation of the nitro group to amino (85%) and carbamoylation by Ph (5-methylisoxazol-3-yl)carbamate (81%) gave II.

ACCESSION NUMBER: 2004:817889 CAPLUS  
 DOCUMENT NUMBER: 141:332200  
 TITLE: N,N'-Di(hetero)aryl(thio)ureas useful as positive allosteric modulators of the α7 subunit of the nicotinic acetylcholine receptor, and their pharmaceutical compositions, uses, and preparation  
 INVENTOR(S): Rogers, Bruce Nelsen; Piotrowski, David Walter; Margolis, Brandon Jerome; Myers, Jason Kenneth; Groppi, Vincent Edward, Jr.; Rudmann, Daniel Gregory  
 PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA  
 SOURCE: PCT Int. Appl., 82 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English

L9 ANSWER 3 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The present invention relates to compositions and methods to treat diseases or conditions with alpha-7 nicotinic acetylcholine receptor (AChR) full agonists by decreasing levels of tumor necrosis factor-alpha and/or by stimulating vascular angiogenesis.

ACCESSION NUMBER: 2004:633526 CAPLUS  
 DOCUMENT NUMBER: 141:167817  
 TITLE: Treatment of diseases with alpha-7 NACH receptor full agonists  
 INVENTOR(S): Groppi, Vincent Edward, Jr.; Rogers, Bruce Nelsen; Rudmann, Daniel Gregory  
 PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA  
 SOURCE: PCT Int. Appl., 142 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE       |
|---|------|----------|-------------------|------------|
| WO 2004064836   | A2   | 20040805 | WO 2004-IB115     | 20040112   |
| W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GM, GR, GR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, LC, LC, LK, LR, LS, LS, LT, LG, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ |      |          |                   |            |
| PRIORITY APPLN. INFO.:  |      |          | US 2003-441801P   | P 20030122 |
| OTHER SOURCE(S):  |      |          | MARPAT 141:167817 |            |

L9 ANSWER 4 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
AB A review. Atomoxetine (Strattera, Eli Lilly & Co.) is a highly selective noradrenaline reuptake inhibitor and the first nonstimulant medication to be approved for the treatment of attention deficit hyperactivity disorder.  
Currently, nine published clin. trials have documented the safety and efficacy of atomoxetine in the treatment of children, adolescents and adults with attention deficit hyperactivity disorder and data presented throughout the past year of national scientific meetings has further addressed its utility. This article reviews the available information on atomoxetine, accompanied by a discussion of its clin. use.  
ACCESSION NUMBER: 2004:630521 CAPLUS  
DOCUMENT NUMBER: 141:235427  
TITLE: Atomoxetine in the treatment of attention deficit hyperactivity disorder  
AUTHOR(S): Kratochvil, Christopher J.; Vaughan, Brigitte S.; Daughton, Joan M.; Mayfield-Jorgensen, Michelle L.; Burke, William J.  
CORPORATE SOURCE: 985581 Nebraska Medical Center, University of Nebraska  
SOURCE: Medical Center, Omaha, NE, 68198 5581, USA  
Expert Review of Neurotherapeutics (2004), 4(4), 601-611  
CODEN: ERNKAR; ISSN: 1473-7175  
PUBLISHER: Future Drugs Ltd.  
DOCUMENT TYPE: Journal: General Review  
LANGUAGE: English  
REFERENCE COUNT: 45  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 5 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
AB The invention relates to a method of treating nausea, vomiting, retching or any combination thereof in a subject in need of treatment. The method comprises administering to a subject in need of treatment a therapeutically effective amount of a compound that has 5-HT3 receptor antagonist activity and NorAdrenaline Reuptake Inhibitor (NARI) activity. The invention further relates to a method of treating nausea, vomiting, retching or any combination thereof in a subject in need thereof, comprising coadministering to said subject a first amount of a 5-HT3 antagonist and a second amount of a NARI, wherein the first and second  
amts. together comprise a therapeutically effective amount or are each present in a therapeutically effective amount. In addition, the method of the invention comprises administering a NARI alone. A pharmaceutical composition comprising:  
(a) a first amount of a 5-HT3 receptor antagonist; and (b) a second amount of a noradrenaline reuptake inhibitor is also claimed.  
ACCESSION NUMBER: 2004:610068 CAPLUS  
DOCUMENT NUMBER: 141:134099  
TITLE: Method of treating nausea, vomiting, or retching by administering a 5-HT3 receptor antagonist and noradrenaline reuptake inhibitor  
INVENTOR(S): Landau, Steven B.; Miller, Cheryl L.; Thor, Karl  
PATENT ASSIGNEE(S): Dynogen Pharmaceuticals, Inc., USA  
SOURCE: PCT Int. Appl., 66 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2004062624   | A2   | 20040729 | WO 2004-US809   | 20040113   |
| W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GM, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MG, MW, MW, MX, MX, MZ |      |          |                 |            |
| US 2004147510   | A1   | 20040729 | US 2004-757981  | 20040113   |
| PRIORITY APPLN. INFO.:  |      |          | US 2003-440076P | P 20030113 |
|   |      |          | US 2003-492478P | P 20030804 |

OTHER SOURCE(S): MARPAT 141:134099

L9 ANSWER 6 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
AB The invention relates to a method of treating functional bowel disorders in a subject in need of treatment. The method comprises administering to a subject in need of treatment a therapeutically effective amount of a compound that has 5-HT3 receptor antagonist activity and NorAdrenaline Reuptake Inhibitor (NARI) activity. The invention further relates to a method of treating a functional bowel disorder in a subject in need thereof, comprising coadministering to said subject a first amount of a 5-HT3 antagonist and a second amount of a NARI, wherein the first and second  
amts. together comprise a therapeutically effective amount or are each present in a therapeutically effective amount. In addition, the method of the invention comprises administering a NARI alone. The functional bowel disorders which can be treated according to the method of the invention include IBS, functional abdominal bloating, functional constipation and functional diarrhea. A pharmaceutical composition comprising: (a) a first amount of a 5-HT3 receptor antagonist; and (b) a second amount of a noradrenaline reuptake inhibitor is also claimed.  
ACCESSION NUMBER: 2004:610067 CAPLUS  
DOCUMENT NUMBER: 141:134098  
TITLE: Method of treating functional bowel disorders by administering a 5-HT3 receptor antagonist and noradrenaline reuptake inhibitor  
INVENTOR(S): Landau, Steven B.  
PATENT ASSIGNEE(S): Dynogen Pharmaceuticals, Inc., USA  
SOURCE: PCT Int. Appl., 81 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2004062623   | A2   | 20040729 | WO 2004-US807   | 20040113   |
| W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GM, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MG, MW, MW, MX, MX, MZ |      |          |                 |            |
| US 2004147509   | A1   | 20040729 | US 2004-757364  | 20040113   |
| PRIORITY APPLN. INFO.:  |      |          | US 2003-440077P | P 20030113 |
|   |      |          | US 2003-492480P | P 20030804 |

OTHER SOURCE(S): MARPAT 141:134098

L9 ANSWER 7 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
AB A method of treating, preventing, or inhibiting a CNS disorder and/or pain and inflammation or an inflammation-associated disorder in a subject in need of such treatment or prevention provides for treating the subject with duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor or prodrug thereof, wherein the amount of duloxetine, venlafaxine or atomoxetine and the amount of a cyclooxygenase-2 selective inhibitor or prodrug thereof together constitute a CNS disorder, pain and inflammation, or inflammation-associated disorder suppressing treatment, prevention, or inhibition effective amount of the composition. Comps. and pharmaceutical compns. that contain duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor are also disclosed.  
ACCESSION NUMBER: 2004:589414 CAPLUS  
DOCUMENT NUMBER: 141:134107  
TITLE: A method for the treatment, prevention, or inhibition of a CNS disorder and/or pain and inflammation using a combination of duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor and compositions thereof  
INVENTOR(S): Azneric, Stephen P.  
PATENT ASSIGNEE(S): Pharmacia Corporation, USA  
SOURCE: PCT Int. Appl., 208 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2004060356   | A1   | 20040722 | WO 2003-US38751 | 20031206   |
| W: AE, AG, AL, AM, AT, AU, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EC, EE, EE, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ |      |          |                 |            |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| US 2004235925   | A1   | 20041125 | US 2003-727717  | 20031204   |
| PRIORITY APPLN. INFO.:  |      |          | US 2002-433790P | P 20021217 |

OTHER SOURCE(S): MARPAT 141:134107

L9 ANSWER 8 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The major human metabolite of atomoxetine (4-hydroxyatomoxetine) was tested against a panel of receptors and enzymes, and was found to interact with the  $\mu$ ,  $\delta$ , and  $\kappa$ -opioid receptors based upon studies involving both binding and functional assays. 4-Hydroxyatomoxetine was determined to be a partial agonist of the  $\kappa$ -opioid receptor.

ACCESSION NUMBER: 2004:523316 CAPLUS  
 DOCUMENT NUMBER: 141:133514  
 TITLE: Synthesis and biological evaluation of the major metabolite of atomoxetine: elucidation of a partial  $\kappa$ -opioid agonist effect

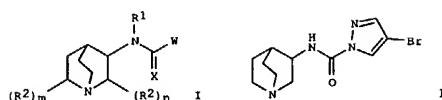
AUTHOR(S): Creighton, Christopher J.; Ramabadran, Kris; Ciccone, Patrick E.; Liu, Jingchun; Orsini, Michael J.; Reitz, Allen B.

CORPORATE SOURCE: Drug Discovery, Research and Development, Johnson and Johnson Pharmaceutical, Spring House, PA, 19477-0776, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(15), 4083-4085  
 CODEN: BMCLB8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 9 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB Title N-[1-azabicyclo[2.2.2]octyl]heteroarylamides I and analogs [wherein X = o, S; R1 = H, (halo)alkyl, cycloalkyl, substituted Ph, naphthyl; R2 = independently halo, cycloalkyl, aryl, (un)substituted alkyl; m = 0-1; n = 0-1; with the proviso that m + n = 1; W = (un)substituted Ph, heterocyclyl, heteroaryl or pharmaceutically acceptable salts, racemic mixts., or pure enantiomers thereof] were prepared as  $\alpha 7$  nicotinic acetylcholine receptor (nAChR) full agonists (no data). For example, reaction of phosgene with 4-bromopyrazole in EtOAc, followed by coupling with (+)-3-aminoquinuclidine-2HCl provided II-HCl (25%). The invention provides for compns. of I with psychostimulants and/or monoamine

reuptake inhibitors for the treatment of attention deficit hyperactivity disorder (ADHD).

ACCESSION NUMBER: 2004:513575 CAPLUS  
 DOCUMENT NUMBER: 141:71755  
 TITLE: Preparation of N-(quinuclidinyl)heteroarylamides as nicotinic acetylcholine receptor agonists for use in combination therapy for the treatment of ADHD

INVENTOR(S): Groppi, Vincent Edward, Jr.; Jacobsen, Eric Jon; Myers, Jason Kenneth; Piotrowski, David Walter; Rogers, Bruce Nelson; Walker, Daniel Patrick; Wishka, Donn Gregory

PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA  
 SOURCE: PCT Int. Appl., 141 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2004052461   | A1   | 20040624 | WO 2003-185542  | 20031128 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD |      |          |                 |          |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |

L9 ANSWER 9 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 PRIORITY APPLN. INFO.: US 2002-432586P P 20021211  
 OTHER SOURCE(S): MARPAT 141:71755

L9 ANSWER 10 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB This invention describes a new combination for the treatment of urinary incontinence and urge urinary incontinence comprising a dual reuptake inhibitor of serotonin and/or - preferably and - norepinephrine and a beta-3-receptor agonist for the treatment of urinary incontinence.

ACCESSION NUMBER: 2004:446890 CAPLUS  
 DOCUMENT NUMBER: 141:12284  
 TITLE: Combination of a  $\beta 3$ -receptor agonist and of a reuptake inhibitor of serotonin and/or norepinephrine for treatment of urinary incontinence

INVENTOR(S): Ebinger, Ursula; Mehlburger, Ludwig; Michel, Martin C.; Wienrich, Marion

PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany  
 SOURCE: Eur. Pat. Appl., 18 pp.  
 CODEN: EPXNDW

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| EP 1424079  | A1   | 20040602 | EP 2002-26546   | 20021127 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK   |      |          |                 |          |
| WO 2004047830   | A2   | 20040610 | WO 2003-EP12225 | 20031103 |
| WO 2004047830   | A3   | 20040819 |                 |          |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD |      |          |                 |          |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
| WO 2004047838   | A2   | 20040610 | WO 2003-EP12331 | 20031105 |
| WO 2004047838   | A3   | 20041028 |                 |          |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD |      |          |                 |          |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |

PRIORITY APPLN. INFO.: EP 2002-26546 A 20021127

L9 ANSWER 11 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB A review. Special considerations arise in treating children and adolescents with antidepressants. Empirical data on antidepressants (and other pharmacol. agents) in young patients are quite limited. Psychiatrists, faced with depriving children of potentially effective medication or prescribing medications "off label," need information on which to base treatment decisions, and efforts are underway (e.g., by the National Institutes of Health, the American Academy of Pediatrics, and the Food and Drug Administration) to promote research in this area. Clin. significant differences in pharmacokinetics and possibly pharmacodynamics between adults and younger patients can also complicate treatment (e.g., younger patients may need higher doses on a milligram-per-kilogram basis to achieve the same drug concentration as an adult on a usually effective adult dose). Younger patients may also be more sensitive to adverse effects of medications. The selective serotonin reuptake inhibitors (SSRIs) have superseded tricyclic antidepressants (TCAs) as first-choice pharmacotherapy based on studies demonstrating their superior safety and efficacy in children with major depressive disorder (MDD). TCAs are now usually reserved for children or adolescents with at least moderate depression who have not responded to at least one newer antidepressant; it is recommended that therapeutic drug monitoring (TDM) of the TCA be done at least once to ensure that the patient does not develop toxic plasma levels. The safety, pharmacokinetics, and tolerability of venlafaxine and nefazodone have been tested in children, but data on efficacy are not yet available. The adverse effect profiles of the SSRIs, the TCAs, venlafaxine, and nefazodone are similar to those in adults. The TCA clomipramine and the SSRIs fluvoxamine and sertraline have indications for obsessive-compulsive disorder in pediatric patients. A number of TCAs and SSRIs have been studied in the treatment of other anxiety disorders (e.g., separation anxiety disorder, school phobia, elective mutism, generalized anxiety disorder) but none has received labeling for those indications. Antidepressants have been studied in the treatment of attention-deficit/hyperactivity disorder (ADHD). The TCA desipramine and bupropion have been found efficacious in ADHD, although desipramine causes higher rates of adverse effects than stimulant medications. Current treatment algorithms generally recommend trying an antidepressant after failed trials of several different stimulant medications. Atomoxetine, a nonstimulant medication, was recently approved for the treatment of ADHD in children, adolescents, and adults. Although behavioral management is preferred for treatment of enuresis, the TCA imipramine has also been found effective, although the relapse rate is as high as 50% upon discontinuation. Given the paucity of data on antidepressants in pediatric patients and the clin. significant pharmacokinetic differences between younger patients and adults, clinicians should carefully consider and cautiously monitor any treatment plan involving antidepressant medications in order to maintain the risk to benefit ratio in favor of the child or adolescent patient.  
ACCESSION NUMBER: 2004:405481 CAPLUS  
DOCUMENT NUMBER: 141:46636  
TITLE: Children and adolescents  
AUTHOR(S): Bober, J. F.; Preskorn, S. H.  
CORPORATE SOURCE: University of Kansas School of Medicine-Wichita,

L9 ANSWER 11 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
Wichita, KS. 67214-3199, USA  
SOURCE: Handbook of Experimental Pharmacology (2004), 157(Antidepressants), 355-378  
CODEN: HEPHD2; ISSN: 0171-2004  
PUBLISHER: Springer-Verlag  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English  
REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L9 ANSWER 12 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB The invention relates generally to the enantiomers of p-hydroxymilnacipran or congeners thereof. Biol. assays revealed that racemic p-hydroxymilnacipran is approx. equipotent in inhibiting serotonin and norepinephrine uptake (IC50 = 28.6 nM for norepinephrine, IC50 = 21.7 nM for serotonin). Interestingly, (+)-p-hydroxymilnacipran is a more potent inhibitor of norepinephrine uptake than serotonin uptake (IC50 = 10.3 nM for norepinephrine, IC50 = 22 nM for serotonin). In contrast, (-)-p-hydroxymilnacipran is a more potent inhibitor of serotonin uptake compared to norepinephrine uptake (IC50 = 88.5 nM for norepinephrine, IC50 = 40.3 nM for serotonin). The invention also relates to salts and prodrug forms of the above compds. In certain embodiments, the compds. of the invention and a pharmaceutically acceptable excipient are combined to prepare a formulation for administration to a patient. Finally, the invention relates to methods of treating mammals suffering from various afflictions, e.g., depression, chronic pain, or fibromyalgia, comprising administering to a mammal in need thereof a therapeutically effective amount of a compound of the invention. Compound preparation is included.  
ACCESSION NUMBER: 2004:392439 CAPLUS  
DOCUMENT NUMBER: 140:400095  
TITLE: Stereoisomers of p-hydroxy-milnacipran, and therapeutic use  
INVENTOR(S): Rariy, Roman V.; Heffernan, Michael; Buchwald, Stephen  
PATENT ASSIGNEE(S): L.; Swager, Timothy M.  
SOURCE: Collegium Pharmaceutical, Inc., USA  
PCT Int. Appl., 163 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO. | DATE       |
|------------------------|--|----------|-----------------|------------|
| WO 2004039320          | A2   | 20040513 | WO 2003-US33681 | 20031022   |
| WO 2004039320          | A3   | 20040624 |                 |            |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW |          |                 |            |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GW, GM, ML, MR, NE, SN, TD, TG   |          |                 |            |
| US 2004142904          | A1   | 20040722 | US 2003-691465  | 20031022   |
| PRIORITY APPLN. INFO.: |  |          | US 2002-421640P | P 20021025 |
|                        |  |          | US 2002-423062P | P 20021101 |
|                        |  |          | US 2003-445142P | P 20030205 |

OTHER SOURCE(S): MARPAT 140:400095

L9 ANSWER 13 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The invention discloses the use of compds. and composition of compds. that  
 that modulate norepinephrine levels for the prevention and treatment of  
 vasomotor symptoms, such as hot flush, caused by, inter alia,  
 thermoregulatory dysfunctions. Compds. of the invention include e.g.  
 desipramine.

ACCESSION NUMBER: 2004:354797 CAPLUS  
 DOCUMENT NUMBER: 140:350606  
 TITLE: Use of norepinephrine reuptake modulators for  
 preventing and treating vasomotor symptoms  
 INVENTOR(S): Deecher, Darlene Coleman; Merchenthaler, Istvan  
 Joseph; Leventhal, Liza; Sipe, Kimberly Jean;  
 O'Connor, Lawrence Thomas  
 PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA  
 SOURCE: PCT Int. Appl., 65 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO. | DATE       |
|------------------------|--|----------|-----------------|------------|
| WO 2004035058          | A1   | 20040429 | WO 2003-US32759 | 20031015   |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EL, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |          |                 |            |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG   |          |                 |            |
| US 2004152710          | A1   | 20040805 | US 2003-685812  | 20031014   |
| PRIORITY APPLN. INFO.: |  |          | US 2002-418591P | P 20021015 |
|                        |  |          | US 2003-685812  | A 20031014 |

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 14 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The invention discloses the use of compds. and compns. of compds. that  
 modulate norepinephrine levels for the treatment of vasomotor symptoms,  
 e.g. thermoregulatory disorders. The invention also discloses the use of  
 compds. and compns. of compds. having norepinephrine reuptake inhibitor  
 (NRI) activity alone or norepinephrine reuptake inhibitor and serotonin  
 reuptake inhibitor (NRI/SRI) dual activity in combination with 5-HT2a  
 receptor antagonist activity.

ACCESSION NUMBER: 2004:354778 CAPLUS  
 DOCUMENT NUMBER: 140:350603  
 TITLE: A method of treating vasomotor symptoms using a  
 compound having norepinephrine reuptake inhibitor  
 activity and 5-HT2a antagonistic activity  
 INVENTOR(S): Deecher, Darlene Coleman; Merchenthaler, Istvan  
 Joseph  
 PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA  
 SOURCE: PCT Int. Appl., 34 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO. | DATE       |
|------------------------|--|----------|-----------------|------------|
| WO 2004035036          | A1   | 20040429 | WO 2003-US32554 | 20031015   |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EL, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |          |                 |            |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG   |          |                 |            |
| US 2004180879          | A1   | 20040916 | US 2003-685974  | 20031014   |
| PRIORITY APPLN. INFO.: |  |          | US 2002-418516P | P 20021015 |
|                        |  |          | US 2003-685974  | A 20031014 |

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 15 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A review. Since attention-deficit/hyperactivity disorder (ADHD) is  
 usually diagnosed in children, evidence from the studies of pharmacol.  
 treatments for children with ADHD is used to inform pharmacol. treatment  
 recommendations for adults. A large percentage of children diagnosed  
 with ADHD have symptoms that persist into adolescence and adulthood. Evidence  
 shows that pharmacol. treatments improve functional outcomes in children  
 with ADHD, and studies using similar pharmacol. treatments show pos.  
 results in adults with ADHD. This article reviews the use of long-acting  
 methylphenidate, mixed amphetamine salts, desipramine, monoamine oxidase  
 inhibitors, bupropion, and atomoxetine in studies of children,  
 adolescents, and adults with ADHD.

ACCESSION NUMBER: 2004:345153 CAPLUS  
 DOCUMENT NUMBER: 140:417062  
 TITLE: ADHD treatment across the life cycle  
 AUTHOR(S): Spencer, Thomas J.  
 CORPORATE SOURCE: Department of Pediatric Psychopharmacology,  
 Massachusetts General Hospital, Department of  
 Psychiatry, Harvard Medical School, Boston, USA  
 SOURCE: Journal of Clinical Psychiatry (2004), 65(Suppl. 3),  
 22-26  
 CODEN: JCLPDE; ISSN: 0160-6689  
 PUBLISHER: Physicians Postgraduate Press, Inc.  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English  
 REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR  
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 16 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The invention provides novel antipsychotic therapies and compns. useful  
 therein and provides methods for identifying new candidate mols. for the  
 treatment of psychosis based on the proportional binding affinities for  
 α2 adrenergic and D2 dopamine receptors.

ACCESSION NUMBER: 2004:101019 CAPLUS  
 DOCUMENT NUMBER: 140:157473  
 TITLE: Antipsychotic combination therapies and compositions  
 of an alpha-2 adrenergic receptor antagonist and an  
 atypical antipsychotic neuroleptic  
 INVENTOR(S): Pickar, David; Wadenberg, Marie-Louise; Svensson,  
 Torgny  
 PATENT ASSIGNEE(S): Potomac, Pharma Inc., USA  
 SOURCE: PCT Int. Appl., 45 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO. | DATE       |
|------------------------|--|----------|-----------------|------------|
| WO 2004011031          | A1   | 20040205 | WO 2003-US23440 | 20030728   |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EL, EC, EE, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |          |                 |            |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG   |          |                 |            |
| US 2004127489          | A1   | 20040701 | US 2003-629123  | 20030728   |
| PRIORITY APPLN. INFO.: |  |          | US 2002-398718P | P 20020729 |
|                        |  |          | US 2002-398719P | P 20020729 |
|                        |  |          | US 2002-398720P | P 20020729 |
|                        |  |          | US 2002-402542P | P 20020812 |
|                        |  |          | US 2002-433781P | P 20021217 |
|                        |  |          | US 2002-433782P | P 20021217 |
|                        |  |          | US 2002-433785P | P 20021217 |

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT



L9 ANSWER 17 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB We present an extension and confirmation of our previously published method for the prediction of volume of distribution (VD) in humans for neutral and basic compounds. It is based on two expl. determined physicochem. parameters, ElogD (7.4) and fi(7.4), the latter being the fraction of compound ionized at pH 7.4, and on the fraction of free drug in plasma (fu). By regressing the fraction unbound in tissues, fu, vs. the above parameters, we demonstrate the ruggedness of the method in predicting VD through the Oie-Tozer equation, via the use of several testing approaches. A comparison is also presented between several methods based on animal pharmacokinetic data, using the same set of proprietary compounds, and it lends further support for the use of this method, as opposed to methods that require the gathering of pharmacokinetic data in laboratory animals. The reduction in the use of animals and the overall faster and cheaper accessibility of the parameters used make this method highly attractive for prospectively predicting the VD of new chemical entities in humans.

ACCESSION NUMBER: 2004:85683 CAPLUS  
 DOCUMENT NUMBER: 140:246128  
 TITLE: Prediction of Human Volume of Distribution Values for Neutral and Basic Drugs. 2. Extended Data Set and Leave-Class-Out Statistics  
 AUTHOR(S): Lombardo, Franco; Obach, R. Scott; Shalaeva, Marina Y.; Gao, Feng  
 CORPORATE SOURCE: Molecular Properties Group, Pharmacokinetics, and Metabolism, and Nonclinical Statistics Group, Pfizer Global Research and Development, Groton Laboratories, Groton, CT, 06340, USA  
 SOURCE: Journal of Medicinal Chemistry (2004), 47(5), 1242-1250  
 CODEN: JMCMAR; ISSN: 0022-2623  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS  
 FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L9 ANSWER 18 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Disclosed is use of reboxetine in combination with a smoking-cessation enhancing agent for promoting smoking cessation. Also disclosed is a composition comprising reboxetine and a smoking-cessation enhancing agent for use for promoting smoking cessation. Examples of the smoking-cessation enhancing agents include nicotine, an antidepressant, a nicotine receptor antagonist, and an opioid antagonist. Examples of compounds are combinations of reboxetine with bupropion.

ACCESSION NUMBER: 2004:20476 CAPLUS  
 DOCUMENT NUMBER: 140:53478  
 TITLE: Method of promoting smoking cessation  
 INVENTOR(S): Wong, Erik H. F.  
 PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA  
 SOURCE: PCT Int. Appl., 21 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2004002463   | A2   | 20040108 | WO 2003-US16232 | 20030626   |
| WO 2004002463   | A3   | 20040219 |                 |            |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GM, GR, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SV, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |            |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| US 2004102440   | A1   | 20040527 | US 2003-602447  | 20030624   |
| PRIORITY APPLN. INFO.:  |      |          | US 2002-392893P | P 20020701 |

L9 ANSWER 19 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Drugs that affect neurotransmitter release can induce changes in neuroregulation during chronic administration. Thus, in addition to recurrence of symptoms of the illness, discontinuation of treatment can be associated with clin. signs and symptoms related to these changes. Atomoxetine, a new drug approved in the United States for treatment of attention deficit/hyperactivity disorder (ADHD), is associated with blockade of the presynaptic norepinephrine transporter. Because treatment of ADHD typically involves chronic treatment, the potential for production of a discontinuation syndrome as well as recurrence of symptoms upon drug discontinuation were assessed as part of the clin. development process. The effects of discontinuation of atomoxetine were assessed in children and adults with ADHD following 9 to 10 wk of continuous therapy in 4 large studies. Symptoms of ADHD worsened following drug discontinuation but did not return to pretreatment levels. The incidence of discontinuation-emergent adverse events was low and there were no statistically significant differences between the patients abruptly discontinuing from atomoxetine and those continuing on placebo. Discontinuation of atomoxetine did not result in the development of an acute discontinuation syndrome and was well tolerated. It appears that atomoxetine may be discontinued without risk for symptom rebound or discontinuation-emergent adverse effects. Tapering of doses is not necessary when atomoxetine is discontinued.

ACCESSION NUMBER: 2004:13455 CAPLUS  
 DOCUMENT NUMBER: 141:133903  
 TITLE: Changes in Symptoms and Adverse Events After Discontinuation of Atomoxetine in Children and Adults With Attention Deficit/Hyperactivity Disorder: A Prospective, Placebo-Controlled Assessment  
 AUTHOR(S): Wernicke, Joachim F.; Adler, Lenard; Spencer, Thomas; West, Scott A.; Allen, Albert J.; Heiligenstein, Milton; Denai, Ruff; Dustin; Brown, W. Jeffrey; Kelsey, Douglas; Michelson, David  
 CORPORATE SOURCE: Lilly Research Laboratories, Indianapolis, IN, USA  
 SOURCE: Journal of Clinical Psychopharmacology (2004), 24(1), 30-35  
 CODEN: JCPYDR; ISSN: 0271-0749  
 PUBLISHER: Lippincott Williams & Wilkins  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS  
 FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L9 ANSWER 20 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The invention provides a method for treating obesity and minimizing metabolic risk factors associated therewith using e.g. zonisamide or other weight loss-promoting anticonvulsants, either alone or in combination with bupropion or other compound that enhances the activity of norepinephrine and/or dopamine via uptake inhibition or other mechanism.

ACCESSION NUMBER: 2003:931170 CAPLUS  
 DOCUMENT NUMBER: 139:391377  
 TITLE: Method using anticonvulsant agents and compounds enhancing norepinephrine and/or dopamine activity for treating obesity  
 INVENTOR(S): Gadde, Kishore M.; Krishnan, K. Ranga R.  
 PATENT ASSIGNEE(S): Duke University, USA  
 SOURCE: PCT Int. Appl., 35 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE        |
|---|------|----------|-----------------|-------------|
| WO 2003097046   | A1   | 20031127 | WO 2003-US15703 | 20030519    |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GM, GR, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |             |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |             |
| US 2004033965   | A1   | 20040219 | US 2003-440404  | 20030519    |
| US 2004198668   | A1   | 20041007 | US 2004-830071  | 20040423    |
| PRIORITY APPLN. INFO.:  |      |          | US 2002-380874P | P 20020517  |
|   |      |          | US 2003-440404  | A1 20030519 |

OTHER SOURCE(S): MARPAT 139:391377  
 REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS  
 FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

AB Background: Atomoxetine is a highly specific presynaptic inhibitor of the noradrenaline (norepinephrine) transporter that was recently approved in the US for the treatment of patients with attention-deficit/hyperactivity disorder (ADHD). Adverse effects on the cardiovascular system, including abnormalities in heart rate, blood pressure, or cardiac rhythm have been associated with several noradrenergic medications. Objective: To further elucidate the magnitude and impact of blood pressure and pulse elevations in patients taking atomoxetine. Study Design: Short-term cardiovascular safety in children, adolescents, and adults with ADHD was assessed in

five randomized, double-blind trials (duration up to 10 wk) with atomoxetine (n = 612) or placebo (n = 474). Long-term cardiovascular safety in children and adolescents (n = 169) was assessed in patients who entered an open-label extension or a blinded continuation following short-term treatment. Methods: Adverse events, blood pressure, sitting pulse, and electrocardiograms (ECGs) were collected throughout the trials. QT intervals were corrected for heart rate by a data-specific correction factor (QTcd; derived from baseline ECGs) as well as standard methods. Results: Atomoxetine treatment was associated with small but statistically significant increases in mean systolic blood pressure in adults and diastolic blood pressure in children and adolescents. Mean pulse rate increased for all atomoxetine treatment groups. The increases in blood pressure and pulse tended to occur early in therapy, stabilized, and returned toward baseline upon drug discontinuation. There was no significant difference between atomoxetine and placebo treatment groups in change in QTcd interval for all study populations. Palpitations in the adult patient population were the only significant cardiovascular adverse event (p = 0.037) occurring more frequently in the atomoxetine treatment group (3.7%) than in the placebo group (0.8%). Discontinuations due to cardiovascular-related events were very uncommon in the adult group, and did not occur in the child/adolescent group. Conclusion: While atomoxetine has noradrenergic activity, increases in pulse and blood pressure were small and of little, if any, clin. significance. Atomoxetine was not associated with QT interval prolongation. Cardiovascular effects of atomoxetine were minimal, and atomoxetine was well tolerated in short- and long-term studies.

ACCESSION NUMBER: 2003:715543 CAPLUS  
DOCUMENT NUMBER: 139:270924  
TITLE: Cardiovascular effects of atomoxetine in children, adolescents, and adults  
AUTHOR(S): Wernicke, Joachim F.; Faries, Douglas; Girod, Donald; Brown, Jeffrey W.; Gao, Haitao; Kelsey, Douglas; Quintana, Humberto; Lipetz, Robert; Michelson, David; Heiligenstein, John  
CORPORATE SOURCE: Lilly Research Laboratories, Indianapolis, IN, USA  
SOURCE: Drug Safety (2003), 26(10), 729-740  
CODEN: DRSAEA; ISSN: 0114-5916  
PUBLISHER: Adis International Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

AB One of the common neurochemical features of many drugs of abuse is their ability to directly or indirectly enhance dopaminergic activity in the brain, particularly within the ventral tegmental-nucleus accumbens pathway. Dopaminergic pathways in the frontal and limbic cortex also may be targets for these agents, where pharmacol. effects could result in heightened attention and/or support self-administration behavior. The purpose of this study was to determine whether drugs from differing pharmacol. classes that exhibit abuse potential would share the ability to counter distractibility in the delayed matching task. Well trained mature macaques performed a computer-assisted delayed matching-to-sample task which included trials associated with three delay intervals and randomly interspersed task-relevant distractors. Drug regimens included four to five doses and subjects were tested no more than twice per wk. All but one of the six compds. (tomoxetine), on average, increased task accuracy

for either non-distractor or distractor trials. It was evident that for several compds., doses required to improve accuracy for non-distractor trials were routinely greater than the doses required to improve accuracy for distractor trials. Data for the individualized Best dose (based upon the subject's optimal level of accuracy during distractor trials) revealed statistically significant distractor-related improvements in task accuracy for the same five compds. The relative efficacy for reversing distractor-induced decrements in task accuracy was estimated by the level of improvement with respect to baseline: nomifensine (31%) > nicotine (22%) ~ morphine (19%) ~ caffeine (19%) ~ methylphenidate (22%) > tomoxetine (9%). Tomoxetine (noradrenergic preferring) was the only compound that did not produce a significant improvement in accuracy. These results provide pharmacol. support for the concept that attentional mechanisms may play an important role in the "environmental" associative aspects of drug seeking behavior, and as such they may provide the basis for treatment strategies aimed at preventing relapse in detoxified addicts.

ACCESSION NUMBER: 2003:674569 CAPLUS  
DOCUMENT NUMBER: 140:139228  
TITLE: Enhanced attention in rhesus monkeys as a common factor for the cognitive effects of drugs with abuse potential  
AUTHOR(S): Bain, John N.; Prendergast, Mark A.; Terry, Alvin V.; Arneric, Stephen P.; Smith, Mark A.; Buccafusco, Jerry  
CORPORATE SOURCE: J. Department of Pharmacology and Toxicology, Alzheimer's Research Center, Medical College of Georgia, Augusta, GA, 30912-2300, USA  
SOURCE: Psychopharmacology (Berlin, Germany) (2003), 169(2), 150-160  
CODEN: PSCHDL; ISSN: 0033-3158  
PUBLISHER: Springer-Verlag  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE

L9 ANSWER 23 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Atomoxetine (Strattera, Eli Lilly & Co.) is a selective noradrenaline reuptake inhibitor that has been studied for use in the treatment of attention-deficit/hyperactivity disorder (ADHD). So far, two open-label and seven randomized, double-blind, placebo-controlled, clin. trials have been published, six in youths and three in adults. Each of these trials has shown a pos. response as measured by the primary efficacy measures, the ADHD-IV Rating Scale (ADHD RS) or the Conners Adult ADHD Rating Scale (CAARS). Atomoxetine has generally been well tolerated. In Nov. of 2002 the FDA approved atomoxetine for use in the US for the treatment of ADHD in children, adolescents and adults. Atomoxetine is the first nonstimulant approved by the FDA for the treatment of ADHD and the first medication approved for the treatment of adult ADHD.

ACCESSION NUMBER: 2003:493353 CAPLUS  
 DOCUMENT NUMBER: 140:53185  
 TITLE: Atomoxetine: a selective noradrenaline reuptake inhibitor for the treatment of attention-deficit/hyperactivity disorder  
 AUTHOR(S): Kratochvil, Christopher J.; Vaughan, Brigitte S.; Harrington, Martin J.; Burke, William J.  
 CORPORATE SOURCE: Department of Psychiatry, University of Nebraska Medical Center, Omaha, 68191-5581, USA  
 SOURCE: Expert Opinion on Pharmacotherapy (2003), 4(7), 1165-1174  
 CODEN: EOPHF7; ISSN: 1465-6566  
 PUBLISHER: Ashley Publications Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 24 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Selective norepinephrine reuptake inhibitors, particularly atomoxetine, reboxetine and 2-alkylthio substituted phenoxypheyl propylamines, are used for the treatment of cognitive failure, including cognitive failure due to dementia, delirium and schizophrenia.

ACCESSION NUMBER: 2003:472376 CAPLUS  
 DOCUMENT NUMBER: 139:30841  
 TITLE: Use of norepinephrine reuptake inhibitors for the treatment of cognitive failure  
 INVENTOR(S): Bymaster, Franklin Porter; Gehlert, Donald Richard; McKinzie, David Lee; Yang, Charles Renkin  
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
 SOURCE: PCT Int. Appl., 31 pp.  
 CODEN: PIXKD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2003049724   | A1   | 20030619 | WO 2002-US36132 | 20021127   |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |            |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| BR 2002013581   | A    | 20040824 | BR 2002-13581   | 20021127   |
| EP 1458368  | A1   | 20040922 | EP 2002-789574  | 20021127   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK   |      |          |                 |            |
| PRIORITY APPLN. INFO.:  |      |          | US 2001-339174P | P 20011211 |
|   |      |          | WO 2002-US36132 | W 20021127 |

OTHER SOURCE(S): MARPAT 139:30841  
 REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 25 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Selective norepinephrine reuptake inhibitors, e.g. atomoxetine, are used to treat tic disorders

ACCESSION NUMBER: 2003:454102 CAPLUS  
 DOCUMENT NUMBER: 139:974  
 TITLE: Use of norepinephrine reuptake inhibitors for the treatment of tic disorders  
 INVENTOR(S): Allen, Albert John; Michelson, David  
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
 SOURCE: PCT Int. Appl., 23 pp.  
 CODEN: PIXKD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2003047560   | A1   | 20030612 | WO 2002-US33628 | 20021112   |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |            |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| EP 1455770  | A1   | 20040915 | EP 2002-784195  | 20021112   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK   |      |          |                 |            |
| PRIORITY APPLN. INFO.:  |      |          | US 2001-334494P | P 20011130 |
|   |      |          | WO 2002-US33628 | W 20021112 |

OTHER SOURCE(S): MARPAT 139:974  
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 26 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A process for producing an optically active amino alc. is provided that includes a step in which a nitro ketone or a cyano ketone is reacted with a hydrogen-donating organic or inorg. compound in the presence of a transition metal compound catalyst having an optically active nitrogen-containing compound as an asym. ligand to give an optically active nitro alc. or an optically active cyano alc., and a step in which the above optically active alc. is further reduced to efficiently produce an optically active amino alc. Thus, PhCOCH2CN was reduced with HCO2H in presence of Et3N and chloro[(S,S)-N-(p-toluenesulfonyl)-1,2-diphenylethylenediamine](p-cymene)ruthenium to give (S)-HOCHPhCH2CN in 98% ee. This compound was reduced with BH3.Me2S to give (S)-HOCHPhCH2CH2NH2 with 98% ee. The alcs. are intermediates for pharmaceuticals, such as fluoxetine, tomoxetine, nisoxetine and norfluoxetine.

ACCESSION NUMBER: 2003:356091 CAPLUS  
 DOCUMENT NUMBER: 138:353733  
 TITLE: Process for producing optically active amino alcohols  
 INVENTOR(S): Watanabe, Masahito; Murata, Kunihiko; Ikariya, Takao  
 PATENT ASSIGNEE(S): Kanto Kagaku Kabushiki Kaisha, Japan  
 SOURCE: Eur. Pat. Appl., 23 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| EP 1308435  | A2   | 20030507 | EP 2002-24517   | 20021030   |
| EP 1308435  | A3   | 20030604 |                 |            |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK |      |          |                 |            |
| JP 2003201269   | A2   | 20030718 | JP 2002-251994  | 20020829   |
| JP 3504254  | B2   | 20040308 |                 |            |
| CA 2409906  | AA   | 20030430 | CA 2002-2409906 | 20021028   |
| JP 2003201270   | A2   | 20030718 | JP 2002-316217  | 20021030   |
| US 2003171592   | A1   | 20030911 | US 2002-285164  | 20021031   |
| US 6686505  | B2   | 20040203 |                 |            |
| PRIORITY APPLN. INFO.:  |      |          | JP 2001-335322  | A 20011031 |
|   |      |          | JP 2002-251994  | A 20020829 |

OTHER SOURCE(S): MARPAT 138:353733

L9 ANSWER 27 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB Buccal aerosol sprays or capsules using polar and non-polar solvent have  
now been developed which provide biol. active compds. for rapid  
absorption  
through the oral mucosa, resulting in fast onset of effect. The buccal  
polar compns. of the invention comprise formulation A: aqueous polar  
solvent,  
active compound, and optional flavoring agent; formulation B: aqueous  
polar  
solvent, active compound, optionally flavoring agent, and propellant;  
formulation C: non-polar solvent, active compound, and optional flavoring  
agent; and formulation D: non-polar solvent, active compound, optional  
flavoring agent, and propellant. Thus, a lingual spray contained  
sumatriptan succinate 10-15, EtOH 10-20, propylene glycol 10-15, PEG  
35-40, water 10-15, and flavors 2-3%.

ACCESSION NUMBER: 2003:319255 CAPLUS  
DOCUMENT NUMBER: 138:343854  
TITLE: Buccal sprays or capsules containing drugs for  
treating disorders of the central nervous system  
INVENTOR(S): Dugger, Harry A.  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.--in-part of U.S.  
Ser. No. 537,118.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 14  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| US 2003077227   | A1   | 20030424 | US 2002-230060  | 20020829 |
| WO 9916417  | A1   | 19990408 | WO 1997-US17899 | 19971001 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM   |      |          |                 |          |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
| EP 1029536  | A1   | 20000823 | EP 2000-109347  | 19971001 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |      |          |                 |          |
| EP 1036561  | A1   | 20000920 | EP 2000-109357  | 19971001 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |      |          |                 |          |
| WO 2004035021   | A2   | 20040429 | WO 2003-US26847 | 20030827 |
| WO 2004035021   | A3   | 20041111 |                 |          |
| W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, NR, NE, SN, TD, TG  |      |          |                 |          |
| US 2004141923   | A1   | 20040722 | US 2003-671720  | 20030929 |

L9 ANSWER 28 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB The invention discloses the use of inhibitors of the noradrenaline  
reuptake system for the production of a medicament for the treatment of  
motor  
inefficiency or increasing the efficiency of motor learning.

ACCESSION NUMBER: 2003:279592 CAPLUS  
DOCUMENT NUMBER: 138:265676  
TITLE: Noradrenaline reuptake inhibitors for increasing the  
effectiveness of motor learning  
INVENTOR(S): Gerloff, Christian; Flewma, Christian  
PATENT ASSIGNEE(S): Germany  
SOURCE: Ger. Offen., 4 pp.  
CODEN: GWXXBX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO.  | DATE        |
|------------------------|------|----------|------------------|-------------|
| DE 10244537            | A1   | 20030410 | DE 2002-10244537 | 20020925    |
| PRIORITY APPLN. INFO.: |      |          | DE 2001-10147383 | IA 20010926 |

L9 ANSWER 27 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
US 2004120895 A1 20040624 US 2003-726585 20031204  
PRIORITY APPLN. INFO.: WO 1997-US17899 A2 19971001  
US 2000-537118 A2 20000329  
EP 1997-911621 A3 19971001  
US 2002-230060 A 20020829

L9 ANSWER 29 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB A pharmaceutical composition comprising a polypeptide and an active agent  
attached to said polypeptide is disclosed.

ACCESSION NUMBER: 2003:202410 CAPLUS  
DOCUMENT NUMBER: 138:226705  
TITLE: Novel pharmaceuticals comprising drug conjugates with  
polypeptide carriers  
INVENTOR(S): Picariello, Thomas  
PATENT ASSIGNEE(S): New River Pharmaceuticals Inc., USA  
SOURCE: PCT Int. Appl., 2059 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 11  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2003020200   | A2   | 20030313 | WO 2001-US43117 | 20011116   |
| WO 2003020200   | A3   | 20030912 |                 |            |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW |      |          |                 |            |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| EP 1357928  | A2   | 20031105 | EP 2001-273387  | 20011116   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                 |            |
| PRIORITY APPLN. INFO.:  |      |          | US 2000-248600P | P 20001116 |
|   |      |          | US 2000-248601P | P 20001116 |
|   |      |          | US 2000-248603P | P 20001116 |
|   |      |          | US 2000-248604P | P 20001116 |
|   |      |          | US 2000-248606P | P 20001116 |
|   |      |          | US 2000-248607P | P 20001116 |
|   |      |          | US 2000-248608P | P 20001116 |
|   |      |          | US 2000-248609P | P 20001116 |
|   |      |          | US 2000-248611P | P 20001116 |
|   |      |          | US 2000-248689P | P 20001116 |
|   |      |          | US 2000-248691P | P 20001116 |
|   |      |          | US 2000-248692P | P 20001116 |
|   |      |          | US 2000-248693P | P 20001116 |
|   |      |          | US 2000-248694P | P 20001116 |

L9 ANSWER 29 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 US 2000-248695P P 20001116  
 US 2000-248696P P 20001116  
 US 2000-248697P P 20001116  
 US 2000-248698P P 20001116  
 US 2000-248701P P 20001116  
 US 2000-248702P P 20001116  
 US 2000-248703P P 20001116  
 US 2000-248704P P 20001116  
 US 2000-248705P P 20001116  
 US 2000-248706P P 20001116  
 US 2000-248707P P 20001116  
 US 2000-248708P P 20001116  
 US 2000-248709P P 20001116  
 US 2000-248710P P 20001116  
 US 2000-248711P P 20001116  
 US 2000-248712P P 20001116  
 US 2001-248664P P 20011116  
 US 2001-248665P P 20011116  
 US 2001-248666P P 20011116  
 US 2001-248667P P 20011116  
 US 2001-248668P P 20011116  
 US 2001-248669P P 20011116  
 US 2001-248671P P 20011116  
 US 2001-248672P P 20011116  
 US 2001-248673P P 20011116  
 US 2001-248674P P 20011116  
 US 2001-248675P P 20011116  
 US 2001-248676P P 20011116  
 US 2001-248677P P 20011116  
 US 2001-248678P P 20011116

L9 ANSWER 29 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 US 2001-248679P P 20011116  
 US 2001-248680P P 20011116  
 US 2001-248681P P 20011116  
 US 2001-248682P P 20011116  
 US 2001-248683P P 20011116  
 US 2001-248684P P 20011116  
 US 2001-248765P P 20011116  
 US 2001-248766P P 20011116  
 US 2001-248767P P 20011116  
 US 2001-248773P P 20011116  
 US 2001-248774P P 20011116  
 US 2001-248775P P 20011116  
 US 2001-248778P P 20011116  
 US 2001-248780P P 20011116  
 US 2001-248781P P 20011116  
 US 2001-248783P P 20011116  
 US 2001-248784P P 20011116  
 US 2001-248785P P 20011116  
 US 2001-248786P P 20011116  
 US 2001-248787P P 20011116  
 US 2001-248790P P 20011116  
 US 2001-248791P P 20011116  
 US 2001-248792P P 20011116  
 US 2001-248793P P 20011116  
 US 2001-248833P P 20011116  
 US 2001-248848P P 20011116  
 US 2001-248849P P 20011116  
 WO 2001-US43117 W 20011116

L9 ANSWER 30 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A review. Atomoxetine, a norepinephrine reuptake inhibitor, is the first nonstimulant agent approved for the treatment of ADHD. It has been approved for use in pediatric and adult patients. Atomoxetine improves ADHD symptom severity vs. placebo, as evaluated by the ADHD Rating Scale (ADHD RS), and its efficacy appears comparable to immediate-release (IR) methylphenidate. Atomoxetine requires dosage titration and may be administered once or twice daily. Common side effects seen in both pediatric and adult patients include nausea, decreased appetite, and dizziness. Dosage adjustments are necessary for patients receiving atomoxetine and cytochrome P 450 2D6 inhibitors. Based on average wholesale price (AWP), atomoxetine is more costly than existing ADHD therapies. Atomoxetine provides an alternative ADHD therapy for patients who may fail or cannot tolerate conventional treatments.  
 2003:177424 CAPLUS  
 138:348232  
 A nonstimulant therapeutic option for children and adults with attention-deficit hyperactivity disorder  
 Baldinger, Sandra L.; Yogman, Michael W.  
 Provider Service Network, Boston, MA, USA  
 Formulary (2003), 38(2), 85-86, 92, 95-100  
 CODEN: FORMF9; ISSN: 1082-801X  
 Advanstar Communications, Inc.  
 Journal; General Review  
 English  
 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 31 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A review. There has been substantial development of pharmacol. treatments for attention-deficit hyperactivity disorder (ADHD) recently. The greatest change is the approval of new delivery systems for methylphenidate (MPH) and amphetamine (AMP) that permit once a day dosing. There are also a number of new compds. under development for the disorder, including several non-stimulant agents. These compds. target the noradrenergic, histaminergic and dopaminergic systems. The recent developments in the pharmacol. treatment of ADHD should increase therapeutic options and the percentage of individuals with the disorder who can be effectively treated.  
 2003:157384 CAPLUS  
 139:254495  
 Drugs under investigation for attention-deficit hyperactivity disorder  
 Schweitzer, Julie B.; Holcomb, Henry H.  
 Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, 21228, USA  
 Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2002), 3(8), 1207-1211  
 CODEN: COIDAZ; ISSN: 1472-4472  
 PharmaPress Ltd.  
 Journal; General Review  
 English  
 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 32 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A method for prevention and/or treatment of ADHD in a patient in need thereof, the method comprising administering to the patient an effective amount of 2-amino-4,5,6,7-tetrahydro-6-n-propylaminobenzothiazole or a pharmaceutically acceptable acid addition salt, hydrate, or solvate thereof.

ACCESSION NUMBER: 2003:133945 CAPLUS  
 DOCUMENT NUMBER: 138:163585  
 TITLE: Pramipexole for the treatment of ADHD  
 INVENTOR(S): Reess, Juergen; Borsini, Franco  
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany  
 SOURCE: U.S. Pat. Appl. Publ., 5 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO.  | DATE     |
|---------------|------|----------|------------------|----------|
| US 2003036555 | A1   | 20030220 | US 2002-198480   | 20020718 |
| DE 10137633   | A1   | 20030220 | DE 2001-10137633 | 20010803 |
| WO 2003013520 | A1   | 20030220 | WO 2002-EP8500   | 20020731 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1416930 A1 20040512 EP 2002-762417 20020731  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK  
 DE 2001-10137633 A 20010803

PRIORITY APPLN. INFO.:  
 US 2001-312241P P 20010814  
 WO 2002-EP8500 W 20020731

L9 ANSWER 33 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The present invention relates to materials and methods for treating neurologic diseases and disorders including but not limited to epilepsy and autism, as well as general cognitive problems. Preferred compounds include carnosine and homocarnosine and N-acetyl, methylated (anserine, ophidine), decarboxylated (carcinine) and tauryl derivs. of carnosine and homocarnosine.

ACCESSION NUMBER: 2003:133030 CAPLUS  
 DOCUMENT NUMBER: 138:163577  
 TITLE: Improving neurological functions  
 INVENTOR(S): Chez, Michael G.  
 PATENT ASSIGNEE(S): Carn-Aware LLC, USA  
 SOURCE: PCT Int. Appl., 74 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2003013514 | A1   | 20030220 | WO 2002-US22341 | 20020715 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:  
 US 2001-310710P P 20010808  
 US 2001-325136P P 20010927

OTHER SOURCE(S): MARPAT 138:163577  
 REFERENCE COUNT: 6  
 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 34 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The invention provides improved formulations and methods for the treatment of neurologic disorders. A method is described for decreasing inter-individual variability due to CYP2D6-mediated metabolism in the inhibition of norepinephrine uptake by administering to a human that is a CYP2D6 extensive metabolizer an effective amount of atomoxetine in combination with an inhibitor of CYP2D6.

ACCESSION NUMBER: 2003:133010 CAPLUS  
 DOCUMENT NUMBER: 138:163575  
 TITLE: Combination therapy for the treatment of neurological disorders  
 INVENTOR(S): Allen, Albert John; Michelson, David; Sauer, John-Michael; Withers, Jennifer Wright  
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
 SOURCE: PCT Int. Appl., 29 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2003013492 | A1   | 20030220 | WO 2002-US21294 | 20020726 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1423104 A1 20040602 EP 2002-756386 20020726  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK  
 US 2004176466 A1 20040909 US 2004-484646 20040122  
 US 2001-310981P P 20010808

PRIORITY APPLN. INFO.:  
 WO 2002-US21294 W 20020726

REFERENCE COUNT: 2  
 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 35 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Atomoxetine is a nonstimulant drug being studied for the treatment of attention-deficit/hyperactivity disorder (ADHD). Atomoxetine is a highly specific inhibitor of the presynaptic norepinephrine transporter with minimal affinity for other noradrenergic receptors or other neurotransmitter transporters or receptors. Results of a proof-of-concept studies are reported that tested the hypothesis that a selective inhibitor of presynaptic norepinephrine uptake would be effective for the treatment of ADHD in school-aged children. Two identical 12-wk, stratified, randomized, double-blind, placebo-controlled trials were conducted in children who met DSM-IV criteria for ADHD. The primary efficacy outcome measure was the mean change from baseline to endpoint in the Attention-Deficit/Hyperactivity Disorder Rating Scale (ADHD RS) total score. Secondary efficacy measures included the Clin. Global Impressions-ADHD-Severity (CGI-ADHD-S) and the Conners' Parent Rating Scale-Revised: Short Form (CPRS-RS). A total of 291 patients were randomized in the 2 trials combined (Study 1, N = 147; Study 2, N = 144). Stimulant-naïve patients were randomized to atomoxetine, placebo, or methylphenidate. Patients with prior stimulant exposure were randomized to atomoxetine or placebo. Atomoxetine significantly reduced ADHD RS total scores compared with placebo in each study (p < .001). Changes in the CGI-ADHD-S (Study 1: p = .003; Study 2: p = .001) and CPRS-ADHD Index (Study 1: p = .023; Study 2: p < .001) also showed atomoxetine to be statistically significantly superior to placebo in reducing ADHD symptoms. Atomoxetine was found to be well tolerated in this population of pediatric patients. Two studies of atomoxetine early in its development confirmed that atomoxetine, a specific and selective inhibitor of noradrenergic uptake, was effective for the treatment of children with ADHD. In addition, atomoxetine was found to be well tolerated.

ACCESSION NUMBER: 2003:90776 CAPLUS  
 DOCUMENT NUMBER: 138:180579  
 TITLE: Results from 2 proof-of-concept, placebo-controlled studies of atomoxetine in children with attention-deficit/hyperactivity disorder  
 AUTHOR(S): Spencer, Thomas; Heiligenstein, John H.; Biederman, Joseph; Faries, Douglas E.; Kratochvil, Christopher J.; Conners, C. Keith; Potter, William Z.  
 CORPORATE SOURCE: Massachusetts General Hospital, Boston, USA  
 SOURCE: Journal of Clinical Psychiatry (2002), 63(12), 1140-1147  
 CODEN: JCLPDE; ISSN: 0160-6689  
 PUBLISHER: Physicians Postgraduate Press, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 31  
 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 36 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Background: Attention-deficit/hyperactivity disorder (ADHD) has been less studied in adults than in children, and the treatment studies reported to date have been small, single-center trials. To assess the efficacy of atomoxetine, a new and highly selective inhibitor of the norepinephrine transporter, we conducted two large, multicenter treatment trials. Methods: Two identical studies using randomized, double-blind, placebo-controlled designs and a 10-wk treatment period were conducted in adults with DSM-IV-defined ADHD as assessed by clin. history and confirmed by a structured interview (study I, n = 280; study II, n = 256). The primary outcome measure was a comparison of atomoxetine and placebo using repeated measures mixed model anal. of postbaseline values of the Conners' Adult ADHD Rating Scale. Results: In each study, atomoxetine was statistically superior to placebo in reducing both inattentive and hyperactive and impulsive symptoms as assessed by primary and secondary measures. Discontinuations for adverse events among atomoxetine patients were under 10% in both studies. Conclusions: Atomoxetine appears to be an efficacious treatment for adult ADHD. Its lack of abuse potential may be an advantage for many patients.

ACCESSION NUMBER: 2003:53172 CAPLUS  
 DOCUMENT NUMBER: 139:240117  
 TITLE: Atomoxetine in adults with ADHD: two randomized, placebo-controlled studies  
 AUTHOR(S): Michelson, David; Adler, Lenard; Spencer, Thomas; Reimherr, Frederick W.; West, Scott A.; Allen, Albert J.; Kelsey, Douglas; Wernicke, Joachim; Dietrich, Anthony; Milton, Denai  
 CORPORATE SOURCE: Lilly Research Laboratories, Indianapolis, IN, USA  
 SOURCE: Biological Psychiatry (2003), 53(2), 112-120  
 CODEN: BIPCBF; ISSN: 0006-3223  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS  
 FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L9 ANSWER 37 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB A review. Atomoxetine is a selective norepinephrine reuptake inhibitor that is being developed for the treatment of attention deficit/hyperactivity disorder (ADHD). Atomoxetine will be the first nonstimulant medication approved by the U.S. Food and Drug Administration (FDA) for the treatment of ADHD. Throughout the testing phases, more than 2000 children and adolescents have been exposed to atomoxetine in clin. trials, with both the number of exposures and the length of exposure time increasing. Serious adverse events have not been clearly associated with the drug, and there have been few discontinuations due to adverse events. The most common drug-related event reported in trials has been decreased appetite and an initial period of weight loss followed by an apparently normal rate of weight gain. These events tend to appear early in the course of treatment with atomoxetine and then decline. Atomoxetine has also been associated with mild increases in blood pressure and pulse that plateau during treatment and resolve upon discontinuation. There have been no effects seen on the QT interval, and the cytochrome P 450 2D6 metabolism of patients seems to have little effect on safety or tolerability of the drug. This article will review the data from completed and ongoing clin. trials available at the time the New Drug Application was submitted to the FDA. Described are serious adverse events, discontinuations, and treatment-emergent adverse events. Specifically, cardiac effects and effects on weight, height, and metabolism that are related to treatment of ADHD with atomoxetine in children and adolescents are discussed.

ACCESSION NUMBER: 2003:2271 CAPLUS  
 DOCUMENT NUMBER: 138:49290  
 TITLE: Safety profile of atomoxetine in the treatment of children and adolescents with ADHD  
 AUTHOR(S): Wernicke, J. F.; Kratochvil, Christopher J.  
 CORPORATE SOURCE: Eli Lilly and Company, Indianapolis, IN, USA  
 SOURCE: Journal of Clinical Psychiatry (2002), 63(Suppl. 12), 50-55  
 CODEN: JCLPDE; ISSN: 0160-6689  
 PUBLISHER: Physicians Postgraduate Press, Inc.  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English  
 REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS  
 FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L9 ANSWER 38 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB A review. Optimal medications for children with attention-deficit/hyperactivity disorder (ADHD) would be effective, well tolerated, and long acting and not cause mood swings or worsen comorbid conditions. Current medications work on brain dopamine and/or norepinephrine systems, which are thought to be involved in ADHD. The medication class with the most evidence of efficacy in ADHD is stimulants, but they may be abused, are effective for only 4 to 12 h, and may cause mood swings or increase tic severity. In recent years, alternative treatments have been explored. Tricyclic antidepressants have efficacy comparable to that of stimulants but may cause constipation, dry mouth, tremors, blood pressure changes, and potentially serious side effects including cardiac conduction and repolarization delays. Monoamine oxidase inhibitors may improve ADHD symptoms but are associated with severe dietary restrictions. Serotonin reuptake inhibitors have little or no effect in ADHD but may improve comorbid depression. Bupropion, although less effective than stimulants, may improve both ADHD symptoms and comorbid depression. Antihypertensive agents may improve impulsivity, hyperactivity, and comorbid tics but cause sedation or rebound hypertension. Atomoxetine, which is being developed for ADHD, reduces symptoms of ADHD without exacerbating comorbid conditions and is associated with only minor side effects, including subtle changes in blood pressure and heart rate. Before prescribing a treatment, physicians should consider the appropriateness and effectiveness of any medication for children with ADHD, who may be less tolerant of side effects and less able to monitor and express concerns about their well-being than adults.

ACCESSION NUMBER: 2003:2270 CAPLUS  
 DOCUMENT NUMBER: 138:49289  
 TITLE: Novel treatments for attention-deficit/hyperactivity disorder in children  
 AUTHOR(S): Spencer, Thomas J.; Biederman, Joseph; Wilens, Timothy  
 CORPORATE SOURCE: E.; Faraone, Stephen V.  
 SERVICE: Pediatric Psychopharmacology Unit, Department of Psychiatry, Harvard Medical School, Psychiatry  
 SOURCE: Massachusetts General Hospital, Boston, USA  
 SOURCE: Journal of Clinical Psychiatry (2002), 63(Suppl. 12), 16-22  
 CODEN: JCLPDE; ISSN: 0160-6689  
 PUBLISHER: Physicians Postgraduate Press, Inc.  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English  
 REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS  
 FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L9 ANSWER 39 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB The purpose of this study was to characterize the effect of potent CYP2D6 inhibition by paroxetine on atomoxetine disposition in extensive metabolizers. This was a single-blind, two-period, sequential study in healthy individuals. In period 1, 20 mg atomoxetine bid was administered to steady state. In period 2, 20 mg paroxetine was administered qd for 22 days. On days 12 through 17, 20 mg atomoxetine bid were coadministered. Plasma pharmacokinetics of atomoxetine, 4-hydroxyatomoxetine, and N-desmethyatomoxetine was determined at steady state in each treatment period. Plasma pharmacokinetics of paroxetine were determined after the 11th and 17th doses. Paroxetine increased C<sub>ss,max</sub>, AUC<sub>0-12</sub>, and t<sub>1/2</sub> of atomoxetine by approx. 3.5-, 6.5-, and 2.5 fold, resp. After coadministration with paroxetine, increases in N-desmethyatomoxetine and decreases in 4-hydroxyatomoxetine concns. were observed. No changes in paroxetine pharmacokinetics were observed after coadministration with atomoxetine. It was concluded that inhibition of CYP2D6 by paroxetine markedly affected atomoxetine disposition, resulting in pharmacokinetics similar to poor metabolizers of CYP2D6 substrates.

ACCESSION NUMBER: 2002:884652 CAPLUS  
 DOCUMENT NUMBER: 139:46424  
 TITLE: Effect of potent CYP2D6 inhibition by paroxetine on atomoxetine pharmacokinetics  
 AUTHOR(S): Belle, Donna J.; Ernest, C. Steven; Sauer, John-Michael; Smith, Brian P.; Thomasson, Holly R.; Witcher, Jennifer W.  
 CORPORATE SOURCE: Departments of Clinical Pharmacology, Drug Disposition, and Global Pharmacokinetics/Pharmacodynam  
 SOURCE: ICS, Eli Lilly and Company, Indianapolis, IN, USA  
 SOURCE: Journal of Clinical Pharmacology (2002), 42(11), 1219-1227  
 CODEN: JCPCBR; ISSN: 0091-2700  
 PUBLISHER: Sage Publications  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS  
 FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L9 ANSWER 40 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
AB The selective norepinephrine (NE) transporter inhibitor atomoxetine  
(formerly called tomoxetine or LY1395603) has been shown to alleviate  
symptoms in Attention Deficit/Hyperactivity Disorder (ADHD). We  
investigated the mechanism of action of atomoxetine in ADHD by evaluating  
the interaction of atomoxetine with monoamine transporters the effects on  
extracellular levels of monoamines, and the expression of the neuronal  
activity marker Fos in brain regions. Atomoxetine inhibited binding of  
radioligands to clonal cell lines transfected with human NE, serotonin  
(5-HT) and dopamine (DA) transporters with dissociation constants (K<sub>i</sub>)

values of 5, 77 and 1451 nM, resp., demonstrating selectivity for NE transporters.  
In microdialysis studies, atomoxetine increased extracellular (EX) levels  
of NE in prefrontal cortex (PFC) 3-fold, but did not alter 5-HT levels.  
Atomoxetine also increased DAEX concns. in PFC 3-fold, but did not alter  
DAEX in striatum or nucleus accumbens. In contrast, the psychostimulant  
methylphenidate, which is used in ADHD therapy, increased NEEX and DAEX  
equally in PFC, but also increased DAEX in the striatum and nucleus  
accumbens to the same level. The expression of the neuronal activity  
marker Fos was increased 3.7-fold in PFC by atomoxetine administration,  
but was not increased in the striatum or nucleus accumbens, consistent  
with the regional distribution of increased DAEX. We hypothesize that

the atomoxetine-induced increase of catecholamines in PFC, a region involved  
in attention and memory, mediates the therapeutic effects of atomoxetine  
in ADHD. In contrast to methylphenidate, atomoxetine did not increase DA  
in striatum or nucleus accumbens, suggesting it would not have motoric or  
drug abuse liabilities.

ACCESSION NUMBER: 2002:878171 CAPLUS  
DOCUMENT NUMBER: 139:750  
TITLE: Atomoxetine increases extracellular levels of  
norepinephrine and dopamine in prefrontal cortex of  
rat: a potential mechanism for efficacy in Attention  
Deficit/Hyperactivity Disorder  
AUTHOR(S): Bymaster, Frank P.; Katner, Jason S.; Nelson, David  
L.; Hemrick-Luecke, Susan K.; Threlkeld, Penny G.;  
Heiligenstein, John H.; Morin, S. Michelle; Gehlert,  
Donald R.; Perry, Kenneth W.  
CORPORATE SOURCE: Neuroscience Research Division, Lilly Research  
Laboratories, Indianapolis, IN, USA  
SOURCE: Neuropsychopharmacology (2002), 27(5), 699-711  
CODEN: NEUROE; ISSN: 0893-133X  
PUBLISHER: Elsevier Science Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 41 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
AB Methods for treating an individual with a psychiatric order with a  
pharmacol. agent that enhances learning or conditioning in combination  
with a session of psychotherapy are provided. These methods of the  
invention encompass a variety of methods of psychotherapy, and  
psychodynamically oriented psychotherapy, and psychiatric orders  
including

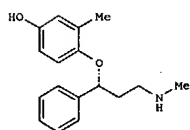
fear and anxiety disorders, addictive disorders, addictive disorders  
including substance-abuse disorders, and mood disorders. The pharmacol.  
agents used for the methods of the present invention are ones that  
generally enhance learning or conditioning, including those that increase  
the level of norepinephrine in the brain, those that increase the level  
of

acetylcholine in the brain, and those that enhance N-methyl-D-aspartate  
(NMDA) receptor transmission in the brain.

ACCESSION NUMBER: 2002:777652 CAPLUS  
DOCUMENT NUMBER: 137:273226  
TITLE: Acute pharmacologic augmentation of psychotherapy  
with  
enhancers of learning or conditioning  
INVENTOR(S): Davis, Michael; Lu, Kwok-Tung; Ressler, Kerry J.  
PATENT ASSIGNEE(S): Emory University, USA  
SOURCE: PCT Int. Appl., 44 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2002078629   | A2   | 20021010 | WO 2002-US9467  | 20020328   |
| WO 2002078629   | A3   | 20021128 |                 |            |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD |      |          |                 |            |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CI, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| CA 2442330  | AA   | 20021010 | CA 2002-2442330 | 20020328   |
| EP 1383465  | A2   | 20040128 | EP 2002-739111  | 20020328   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                 |            |
| JP 2004530666   | T2   | 20041007 | JP 2002-576897  | 20020328   |
| US 2004208923   | A1   | 20041021 | US 2004-473640  | 20040422   |
| PRIORITY APPLN. INFO.:  |      |          | US 2001-279868P | P 20010329 |
|   |      |          | US 2002-363991P | P 20020313 |
|   |      |          | WO 2002-US9467  | W 20020328 |

L9 ANSWER 42 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
GI



AB Pharmaceutically acceptable salts of the monoamine uptake inhibitor,  
(R)-(-)-N-methyl-3-((2-methyl-4-hydroxyphenyl)oxy)-3-phenyl-1-aminopropane  
(II), were prepared. For example, (S)-3-chloro-1-phenylpropanol was  
condensed

with 4-((tert-butoxycarbonyl)oxy)-2-methylphenol in the presence of PPh<sub>3</sub>  
and diisopropylazodicarboxylate in THF to give the aryl ether (85%).  
Iodination with NaI in 2-butanone (91%), followed by amination with MeNH<sub>2</sub>  
and treatment with 0.1N HCl, afforded I-HCl (35%). The latter  
inhibited uptake of both serotonin (K<sub>i</sub> = 43 nM) and norepinephrine (K<sub>i</sub> =  
3.0 nM). An open-label study performed on seven healthy men demonstrated  
that the primary metabolite of

(R)-(-)-N-methyl-3-((2-methylphenyl)oxy)-3-phenyl-1-aminopropane-HCl (II) in both extensive metabolizers (EM) and  
poor metabolizers (PM) of CYP2D6 substrates is I. The EM subjects  
metabolized 86.5% of II, while the PM subjects metabolized 40% of II.  
Formulations of II for treatment of neurol. disorders (no data) are also  
disclosed.

ACCESSION NUMBER: 2002:695931 CAPLUS  
DOCUMENT NUMBER: 137:216750  
TITLE: Preparation of 3-aryloxy-3-phenyl-1-aminopropanes as  
monoamine uptake inhibitors for treatment of  
neurological disorders  
INVENTOR(S): Mattiuz, Edward Louis; Sauer, John-Michael; Wheeler,  
William Joe; Wong, David Taiwai  
PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
SOURCE: PCT Int. Appl., 28 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2002070457   | A1   | 20020912 | WO 2002-US3385  | 20020220 |
| WO 2002070457   | C1   | 20040603 |                 |          |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |          |

L9 ANSWER 43 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN (Continued)  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CI, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GN, GQ, GW, ML, MR, NE, SN, TD, TG

|   |    |          |                 |            |
|---|----|----------|-----------------|------------|
| CA 2440161  | AA | 20020912 | CA 2002-2440161 | 20020220   |
| LU 91038  | A1 | 20030911 | LU 2002-91038   | 20020220   |
| GB 2389851  | A1 | 20031224 | GB 2003-23169   | 20020220   |
| EP 1379492  | A1 | 20040114 | EP 2002-713538  | 20020220   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR |    |          |                 |            |
| EE 200300419  | A  | 20040216 | EE 2003-419     | 20020220   |
| ES 2201942  | A1 | 20040316 | ES 2003-50052   | 20020220   |
| BR 2002007716   | A  | 20040323 | BR 2002-7716    | 20020220   |
| JP 2004525912   | T2 | 20040826 | JP 2002-569778  | 20020220   |
| LT 5143   | B  | 20040625 | LT 2003-75      | 20030811   |
| US 2004082666   | A1 | 20040429 | US 2003-468553  | 20030821   |
| FI 2003001191   | A  | 20030825 | FI 2003-1191    | 20030825   |
| SE 2003002361   | A  | 20030903 | SE 2003-2361    | 20030903   |
| NO 2003003921   | A  | 20031105 | NO 2003-3921    | 20030904   |
| DK 200301267  | A5 | 20031106 | DK 2003-1267    | 20030904   |
| PRIORITY APPLN. INFO.:  |    |          | US 2001-273730P | P 20010306 |
|   |    |          | WO 2002-US3385  | W 20020220 |

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT



L9 ANSWER 43 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A review. Eli Lilly is developing Tomoxetine, a norepinephrine reuptake inhibitor, for the potential treatment of attention deficit hyperactivity disorder (ADHD) and depression. As of May 2000, Tomoxetine was undergoing phase III trials in the US [368128]. An NDA was filed with the FDA in Oct. 2001, with a launch expected in the second half of 2002 [426786]. Tomoxetine was first investigated by Lilly in the 1980s as a potential treatment for depressive illness. The compound was selected from a series of potent inhibitors of norepinephrine reuptake, and reached large-scale phase III clin. trials for depression in 1990. Development for this indication appeared to stop at that time, despite some evidence that Tomoxetine was fairly effective [273943]. In 1996, Lilly apparently restarted preclin. development of Tomoxetine as a potential therapy for ADHD, and submitted EP-00721777 claiming Tomoxetine's utility for this disorder in July of that year [273956]. In June 2001, ABN AMRO predicted sales of \$121 million in 2002, rising to \$4064 million in 2012 [422762]. In Oct. 2001, analysts at Salomon Smith Barney predicted that the product would make sales of \$24 million in 2002, rising to \$305 million in 2005 [427501].

ACCESSION NUMBER: 2002:621921 CAPLUS  
 DOCUMENT NUMBER: 138:180005  
 TITLE: Tomoxetine (Eli Lilly & Co)  
 AUTHOR(S): Preti, Antonio  
 CORPORATE SOURCE: Genneruxi Medical Center, Cagliari, I-09129, Italy  
 SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2002), 3(2), 272-277  
 CODEN: COIDAZ; ISSN: 1472-4472  
 PUBLISHER: PharmaPress Ltd.  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English  
 REFERENCE COUNT: 45  
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 44 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBu)NCA and cephalixin hydrochloride.

ACCESSION NUMBER: 2002:556104 CAPLUS  
 DOCUMENT NUMBER: 137:109489  
 TITLE: Compositions comprising a polypeptide and an active agent  
 INVENTOR(S): Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randal J.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 34 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 11  
 PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE       |
|------------------------|------|----------|-----------------|------------|
| US 2002099013          | A1   | 20020725 | US 2001-933708  | 20010822   |
| US 2004087483          | A1   | 20040506 | US 2002-136433  | 20020502   |
| PRIORITY APPLN. INFO.: |      |          | US 2000-247556P | P 20001114 |
|                        |      |          | US 2000-247558P | P 20001114 |
|                        |      |          | US 2000-247559P | P 20001114 |
|                        |      |          | US 2000-247560P | P 20001114 |
|                        |      |          | US 2000-247561P | P 20001114 |
|                        |      |          | US 2000-247594P | P 20001114 |
|                        |      |          | US 2000-247595P | P 20001114 |
|                        |      |          | US 2000-247606P | P 20001114 |
|                        |      |          | US 2000-247607P | P 20001114 |
|                        |      |          | US 2000-247608P | P 20001114 |
|                        |      |          | US 2000-247609P | P 20001114 |
|                        |      |          | US 2000-247610P | P 20001114 |
|                        |      |          | US 2000-247611P | P 20001114 |
|                        |      |          | US 2000-247612P | P 20001114 |
|                        |      |          | US 2000-247620P | P 20001114 |
|                        |      |          | US 2000-247621P | P 20001114 |
|                        |      |          | US 2000-247634P | P 20001114 |

L9 ANSWER 44 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

|                 |    |          |
|-----------------|----|----------|
| US 2000-247635P | P  | 20001114 |
| US 2000-247698P | P  | 20001114 |
| US 2000-247699P | P  | 20001114 |
| US 2000-247700P | P  | 20001114 |
| US 2000-247701P | P  | 20001114 |
| US 2000-247702P | P  | 20001114 |
| US 2000-247797P | P  | 20001114 |
| US 2000-247798P | P  | 20001114 |
| US 2000-247799P | P  | 20001114 |
| US 2000-247800P | P  | 20001114 |
| US 2000-247801P | P  | 20001114 |
| US 2000-247802P | P  | 20001114 |
| US 2000-247803P | P  | 20001114 |
| US 2000-247804P | P  | 20001114 |
| US 2000-247805P | P  | 20001114 |
| US 2000-247807P | P  | 20001114 |
| US 2000-247832P | P  | 20001114 |
| US 2000-247833P | P  | 20001114 |
| US 2000-247926P | P  | 20001114 |
| US 2000-247927P | P  | 20001114 |
| US 2000-247928P | P  | 20001114 |
| US 2000-247929P | P  | 20001114 |
| US 2000-247930P | P  | 20001114 |
| US 2000-642820  | A2 | 20000822 |
| US 2000-248607P | P  | 20001116 |
| US 2001-933708  | A2 | 20010822 |

L9 ANSWER 45 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB This invention relates to a chemoenzymic process for the stereoselective preparation of both (R) and (S) enantiomers of 3-hydroxy-3-phenylpropanenitrile, useful as a key intermediate for synthesis of (S)-fluoxetine, (R)-tomoxetine and cognant compds., which comprises reacting cyanohydrin with an acetylating agent in the presence of lipase in an organic solvent, followed by separation of (R)-acetate and (S) alc., hydrolyzing (R)-acetate in the presence of potassium carbonate and methanol, filtering the reaction mixture and evaporating the solvent to obtain the (R) alc.

ACCESSION NUMBER: 2002:555676 CAPLUS  
 DOCUMENT NUMBER: 137:108394  
 TITLE: Stereoselective preparation of 3-hydroxy-3-phenylpropanenitrile  
 INVENTOR(S): Kanai, Ahmed; Khanna, Gollapalli Bhasker; Rao, Maddamsetty Venkate; Raghavan, Kondapuram Vijaya  
 PATENT ASSIGNEE(S): Council of Scientific and Industrial Research, India  
 SOURCE: PCT Int. Appl., 14 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2002057475   | A1   | 20020725 | WO 2001-IN8     | 20010122   |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |            |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| GB 2387597  | A1   | 20031022 | GB 2003-17492   | 20010122   |
| GB 2387597  | B2   | 20041110 |                 |            |
| JP 2004520039   | T2   | 20040708 | JP 2002-558527  | 20010122   |
| PRIORITY APPLN. INFO.:  |      |          | WO 2001-IN8     | W 20010122 |

OTHER SOURCE(S): CASREACT 137:108394  
 REFERENCE COUNT: 5  
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 46 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Nondependent light drug users received placebo, atomoxetine (20, 45 and 90 mg) or methylphenidate (20 and 40 mg) in a double-blind, Latin square design. Subjective drug effects were assessed by the Visual Analog Scales (VAS), the Addiction Research Center Inventory (ARCI) and Adjective Rating Scales (ARS). Psychomotor performance was evaluated by the Digit Symbol Substitution Test (DSST). Physiol. measures were also collected throughout the sessions. Assessments were conducted before and 30, 60, 90, 120, 150, 180 and 240 min after drug administration. Forty milligrams methylphenidate produced increases in the stimulant portions of the VAS and ARS and the benzedrine, amphetamine, morphine-benzedrine and lysergic acid diethylamide (LSD) subscales of the ARCI relative to placebo. Ninety mg atomoxetine was reported to be unpleasurable relative to placebo, as indicated by significant increases of the 'bad' and 'sick' portions of the VAS and the LSD subscale of the ARCI. Compared with placebo, both methylphenidate doses increased systolic blood pressure (BP) and heart rate (HR). For atomoxetine, 90 mg increased diastolic BP, 45 and 90 mg increased systolic BP, and all three doses increased HR relative to placebo. Neither compound produced significant differences from placebo on DSST performance. These results suggest that atomoxetine does not induce subjective effects similar to those of methylphenidate and suggest that it is unlikely that atomoxetine will have abuse liability.

ACCESSION NUMBER: 2002:498844 CAPLUS  
 DOCUMENT NUMBER: 138:215131  
 TITLE: Comparison of the subjective, physiological, and psychomotor effects of atomoxetine and methylphenidate in light drug users  
 AUTHOR(S): Heil, S. H.; Holmes, H. W.; Bickel, W. K.; Higgins, S.  
 CORPORATE SOURCE: T.; Badger, G. J.; Laws, H. F.; Faries, D. E. Department of Psychiatry, University of Vermont, Burlington, VT, 05401, USA  
 SOURCE: Drug and Alcohol Dependence (2002), 67(2), 149-156  
 CODEN: DADEDV; ISSN: 0376-8716  
 PUBLISHER: Elsevier Science Ireland Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 35  
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 48 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Selective norepinephrine reuptake inhibitors, e.g. atomoxetine, are used to treat anxiety disorders, especially obsessive-compulsive disorder.

ACCESSION NUMBER: 2002:391520 CAPLUS  
 DOCUMENT NUMBER: 136:363874  
 TITLE: Selective norepinephrine reuptake inhibitors for the treatment of anxiety disorders  
 INVENTOR(S): Thomasson, Holly Read; Michelson, David  
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
 SOURCE: PCT Int. Appl., 20 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 2002040006  | A2   | 20020523 | WO 2001-US27801 | 20011106 |
| WO 2002040006  | A3   | 20031224 |                 |          |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MY, NZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW  |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TG, UG, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM, AT, BE, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MY, NZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW |      |          |                 |          |
| CA 2426069   | AA   | 20020523 | CA 2001-2426069 | 20011106 |
| AU 2002017757  | A5   | 20020527 | AU 2002-17757   | 20011106 |
| EP 1395253   | A2   | 20040310 | EP 2001-996376  | 20011106 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  |      |          |                 |          |
| JP 2004529073  | T2   | 20040924 | JP 2002-542380  | 20011106 |
| US 2004031016  | A1   | 20040219 | US 2003-416294  | 20030507 |
| NO 2003002156  | A    | 20030513 | NO 2003-2156    | 20030513 |
| HR 2003000384  | A1   | 20030931 | HR 2003-384     | 20030514 |
| PRIORITY APPLN. INFO.: US 2000-249010P P 20001115  |      |          |                 |          |
| US 2001-265362P P 20010131   |      |          |                 |          |
| WO 2001-US27801 W 20011106   |      |          |                 |          |

OTHER SOURCE(S): MARPAT 136:363874

L9 ANSWER 47 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The present invention relates to methods for the treatment of diseases associated with hyper-proliferation of cells by administering to a subject in need a therapeutically effective amount of at least one psychotropic agent. Specific proliferative diseases against which psychotropic agents were found to be effective are cancer, including multi-drug resistant cancer and diseases associated with hyper-proliferation of the skin cells, such as psoriasis and hyperkeratosis. Among the examples provided is one demonstrating the effectiveness of topical administration of thioridazine cream on psoriasis in a couple of patients. The effectiveness of psychotropics in inhibiting proliferation of cancer cells and in sensitizing doxorubicin cytotoxicity is demonstrated in various laboratory animal models.

ACCESSION NUMBER: 2002:428639 CAPLUS  
 DOCUMENT NUMBER: 136:395953  
 TITLE: Anti-proliferative drugs  
 INVENTOR(S): Gil-Ad, Irit; Weizman, Abraham  
 PATENT ASSIGNEE(S): Ramot University Authority for Applied Research & Industrial Development Ltd., Israel  
 SOURCE: PCT Int. Appl., 66 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 2002043652  | A2   | 20020606 | WO 2001-IL1105  | 20011129 |
| WO 2002043652  | A3   | 20020723 |                 |          |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MY, NZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM              |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TG, UG, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM, AT, BE, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MY, NZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW |      |          |                 |          |
| CA 2430296   | AA   | 20020606 | CA 2001-2430296 | 20011129 |
| AU 2002018467  | A5   | 20020611 | AU 2002-18467   | 20011129 |
| EP 1347752   | A2   | 20031001 | EP 2001-998305  | 20011129 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  |      |          |                 |          |
| US 2004029860  | A1   | 20040212 | US 2003-432875  | 20030916 |
| PRIORITY APPLN. INFO.: IL 2000-139975 A 20001129   |      |          |                 |          |
| WO 2001-IL1105 W 20011129  |      |          |                 |          |

L9 ANSWER 49 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBt)NCA and cephalixin hydrochloride.

ACCESSION NUMBER: 2002:332011 CAPLUS  
 DOCUMENT NUMBER: 136:355482  
 TITLE: Compositions comprising a polypeptide and an active agent  
 INVENTOR(S): Piccarriello, Thomas; Olson, Lawrence P.; Kirk, Randall J.  
 PATENT ASSIGNEE(S): New River Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 98 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 11  
 PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 2002034237  | A1   | 20020502 | WO 2001-US26142 | 20010822 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MY, NZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM                  |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TG, UG, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM, AT, BE, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MY, NZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW |      |          |                 |          |
| US 6716452   | B1   | 20040406 | US 2000-642820  | 20000822 |
| CA 2420590   | AA   | 20020502 | CA 2001-2420590 | 20010822 |
| AU 2001086599  | A5   | 20020506 | AU 2001-86599   | 20010822 |
| EP 1311242   | A1   | 20030521 | EP 2001-966056  | 20010822 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  |      |          |                 |          |
| JP 2004523480  | T2   | 20040805 | JP 2002-537291  | 20010822 |
| US 2004127397  | A1   | 20040701 | US 2003-727365  | 20031205 |
| PRIORITY APPLN. INFO.: US 2000-642820 A 20000822   |      |          |                 |          |
| US 2000-247613P P 20001114   |      |          |                 |          |
| US 2000-247614P P 20001114   |      |          |                 |          |
| US 2000-247615P P 20001114   |      |          |                 |          |
| US 2000-247616P P 20001114   |      |          |                 |          |
| US 2000-247617P P 20001114   |      |          |                 |          |
| US 2000-247622P P 20001114   |      |          |                 |          |
| US 2000-247630P P 20001114   |      |          |                 |          |
| US 2000-247631P P 20001114   |      |          |                 |          |

L9 ANSWER 49 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 US 2000-247632P P 20001114  
 US 2000-247633P P 20001114  
 US 2000-247556P P 20001114  
 US 2000-247558P P 20001114  
 US 2000-247559P P 20001114  
 US 2000-247560P P 20001114  
 US 2000-247561P P 20001114  
 US 2000-247594P P 20001114  
 US 2000-247595P P 20001114  
 US 2000-247606P P 20001114  
 US 2000-247607P P 20001114  
 US 2000-247608P P 20001114  
 US 2000-247609P P 20001114  
 US 2000-247610P P 20001114  
 US 2000-247611P P 20001114  
 US 2000-247612P P 20001114  
 US 2000-247620P P 20001114  
 US 2000-247621P P 20001114  
 US 2000-247634P P 20001114  
 US 2000-247635P P 20001114  
 US 2000-247698P P 20001114  
 US 2000-247699P P 20001114  
 US 2000-247701P P 20001114  
 US 2000-247702P P 20001114  
 US 2000-247797P P 20001114  
 US 2000-247798P P 20001114  
 US 2000-247799P P 20001114  
 US 2000-247800P P 20001114  
 US 2000-247801P P 20001114  
 US 2000-247802P P 20001114

L9 ANSWER 50 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Good regioselectivity and chirality transfer for aryl-substituted allyl units is achieved in allylic alkylations with a wide range of nucleophiles by using the highly active ruthenium catalyst [CpRu(cod)Cl]. This method provides a route to antidepressants such as (-)-fluoxetine from (S)-ephedrine.  
 ACCESSION NUMBER: 2002:243136 CAPLUS  
 DOCUMENT NUMBER: 137:140298  
 TITLE: A stereospecific ruthenium-catalyzed allylic alkylation  
 AUTHOR(S): Trost, Barry M.; Fraisse, Pierre L.; Ball, Zachary T.  
 CORPORATE SOURCE: Department of Chemistry, Stanford University, Stanford, CA, 94305-5080, USA  
 SOURCE: Angewandte Chemie, International Edition (2002), 41(6), 1059-1061  
 CODEN: AClEF5; ISSN: 1433-7851  
 PUBLISHER: Wiley-VCH Verlag GmbH  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 137:140298

L9 ANSWER 49 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 US 2000-247803P P 20001114  
 US 2000-247804P P 20001114  
 WO 2001-US26142 W 20010822

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 51 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Studies were performed to determine the human enzymes responsible for the biotransformation of atomoxetine to its major metabolite, 4-hydroxyatomoxetine, and to a minor metabolite, N-desmethyatomoxetine. Utilizing human liver microsomes containing a full complement of cytochrome P 450 (P 450) enzymes, average Km and CLint values of 2.3 µM and 103 µl/min/mg, resp., were obtained for 4-hydroxyatomoxetine formation. Microsomal samples deficient in CYP2D6 exhibited average apparent Km and CLint values of 149 µM and 0.2 µl/min/mg, resp. In a human liver bank characterized for P 450 content, formation of 4-hydroxyatomoxetine correlated only to CYP2D6 activity. Of nine expressed P450s examined, 4-hydroxyatomoxetine was formed at a rate 475-fold greater by CYP206 compared with the other P450s. These results demonstrate that CYP2D6 is the enzyme primarily responsible for the formation of 4-hydroxyatomoxetine. Multiple P450s were found to be capable of forming 4-hydroxyatomoxetine when CYP2D6 was not expressed. However, the efficiency at which these enzymes perform this biotransformation is reduced compared with CYP2D6. The formation of the minor metabolite N-desmethyatomoxetine exhibited average Km and CLint values of 83 µM and 0.8 µl/min/mg, resp. Utilizing studies similar to those outlined above, CYP2C19 was identified as the primary enzyme responsible for the biotransformation of atomoxetine to N-desmethyatomoxetine. In summary, CYP2D6 was found to be the primary P 450 responsible for the formation of the major oxidative metabolite of atomoxetine, 4-hydroxyatomoxetine. Furthermore, these studies indicate that in patients with compromised CYP2D6 activity, multiple low-affinity enzymes will participate in the formation of 4-hydroxyatomoxetine. Therefore, coadministration of P 450 inhibitors to poor metabolizers of CYP2D6 substrates would not be predicted to decrease the clearance of atomoxetine in these individuals.  
 ACCESSION NUMBER: 2002:139958 CAPLUS  
 DOCUMENT NUMBER: 137:15251  
 TITLE: Identification of the human cytochromes P450 responsible for atomoxetine metabolism  
 AUTHOR(S): Ring, Barbara J.; Gillespie, Jennifer S.; Eckstein, James A.; Wrighton, Steven A.  
 CORPORATE SOURCE: Department of Drug Disposition, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46205, USA  
 SOURCE: Drug Metabolism and Disposition (2002), 30(3), 319-323  
 CODEN: DMSAI; ISSN: 0090-9556  
 PUBLISHER: American Society for Pharmacology and Experimental Therapeutics  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 52 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB Pharmaceutical compns. are disclosed for the treatment of attention deficit hyperactivity disorder (ADHD). The pharmaceutical compns. are comprised of a therapeutically effective combination of a nicotine receptor partial agonist and an anti-ADHD agent and a pharmaceutically acceptable carrier. The method of using these compds. is also disclosed.  
ACCESSION NUMBER: 2002:104621 CAPLUS  
DOCUMENT NUMBER: 136:145265  
TITLE: A pharmaceutical composition for the treatment of attention deficit hyperactivity disorder (ADHD) comprising a nicotine receptor partial agonist and anti-ADHD agent  
INVENTOR(S): Watsky, Eric Jacob; Coe, Jotham Wadsworth; Harrigan, Edmund Patrick; O'Neill, Brian Thomas; Sands, Steven Bradley  
PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
SOURCE: Eur. Pat. Appl., 19 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE        |
|---|------|----------|-----------------|-------------|
| EP 1177798  | A2   | 20020206 | EP 2001-306455  | 20010727    |
| EP 1177798  | A3   | 20030305 |                 |             |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO |      |          |                 |             |
| US 2002016334   | A1   | 20020207 | US 2001-865793  | 20010525    |
| CA 2354237  | AA   | 20020131 | CA 2001-2354237 | 20010727    |
| BR 2001003169   | A    | 20020528 | BR 2001-3169    | 20010731    |
| JP 2002316949   | A2   | 20020103 | JP 2001-231554  | 20010731    |
| US 2004220184   | A1   | 20041104 | US 2004-851826  | 20040521    |
| PRIORITY APPLN. INFO.:  |      |          | US 2000-221718P | P 20000731  |
|   |      |          | US 2001-865793  | A1 20010525 |

L9 ANSWER 53 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB The present invention pertains to methods for reducing the platelet activation state in an individual comprising administering a selective serotonin reuptake inhibitor (SSRI). The platelet activation state is reduced upon administering a SSRI, as measured by one or more platelet activation markers. The invention also relates to methods for treating or preventing an individual at risk for a vascular event, disease or disorder by administering a SSRI.  
ACCESSION NUMBER: 2002:90620 CAPLUS  
DOCUMENT NUMBER: 136:112659  
TITLE: Methods of inhibiting platelet activation with selective serotonin reuptake inhibitors and treatment of cardiovascular disease  
INVENTOR(S): Seiebruany, Victor L.; Gurbel, Paul A.; O'Connor, Christopher M.  
PATENT ASSIGNEE(S): Heartdrug Research, LLC, USA  
SOURCE: U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. 6,245,782.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE        |
|------------------------|------|----------|-----------------|-------------|
| US 2002013343          | A1   | 20020131 | US 2001-804689  | 20010312    |
| US 6552014             | B2   | 20030422 |                 |             |
| US 6245782             | B1   | 20010612 | US 1999-312987  | 19990517    |
| ZA 2001009994          | A    | 20020826 | ZA 2001-9994    | 20011205    |
| PRIORITY APPLN. INFO.: |      |          | US 1999-312987  | A2 19990517 |

L9 ANSWER 54 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB Norepinephrine reuptake inhibitors, e.g., tomoxetine or its salts, reboxetine, duloxetine, are used to treat psoriasis. Thus, hard gelatin capsules contained tomoxetine-HCl 30.0, starch 305.0, and Mg stearate 5.0 mg/capsule.  
ACCESSION NUMBER: 2001:676591 CAPLUS  
DOCUMENT NUMBER: 135:216029  
TITLE: Treatment of psoriasis with norepinephrine reuptake inhibitors  
INVENTOR(S): Thomasson, Holly Read  
PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
SOURCE: PCT Int. Appl., 18 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2001066101   | A2   | 20010913 | WO 2001-US5260  | 20010220   |
| WO 2001066101   | A3   | 20020207 |                 |            |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |            |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| CA 2400571  | AA   | 20010913 | CA 2001-2400571 | 20010220   |
| EP 1267859  | A2   | 20030102 | EP 2001-918185  | 20010220   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                 |            |
| BR 2001008980   | A    | 20030603 | BR 2001-8980    | 20010220   |
| JP 2003525899   | T2   | 20030902 | JP 2001-564754  | 20010220   |
| ZA 2002005266   | A    | 20031001 | ZA 2002-5266    | 20020701   |
| US 2003045585   | A1   | 20030306 | US 2002-203403  | 20020807   |
| US 6683114  | B2   | 20040127 |                 |            |
| NO 200204236  | A    | 20020905 | NO 2002-4236    | 20020905   |
| PRIORITY APPLN. INFO.:  |      |          | US 2000-187508P | P 20000307 |
|   |      |          | WO 2001-US5260  | W 20010220 |

OTHER SOURCE(S): MARPAT 135:216029

L9 ANSWER 55 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB The present invention provides a method of treating and preventing obesity and related co-morbid conditions comprising the administration of a therapeutically effective amount of one or more monoamine reuptake inhibitors which are serotonin reuptake inhibitors and/or noradrenaline reuptake inhibitors and a 5-HT1A agonist to a patient in need thereof. Monoamine reuptake inhibitors such as sibutramine are useful in treating obesity but have cardiovascular side-effects which can be diminished by administration of a 5-HT1A agonist such as flesinoxan. An example is given in which flesinoxan reduces the cardiovascular (blood pressure, heart rate) effects of sibutramine in rats.  
ACCESSION NUMBER: 2001:635946 CAPLUS  
DOCUMENT NUMBER: 135:190433  
TITLE: Therapeutic agents for treating obesity  
INVENTOR(S): Heal, David John; Cheetham, Sharon Crawford  
PATENT ASSIGNEE(S): Knoll Aktiengesellschaft, Germany  
SOURCE: PCT Int. Appl., 21 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2001062341   | A2   | 20010830 | WO 2001-EP1894  | 20010220   |
| WO 2001062341   | A3   | 20020131 |                 |            |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |            |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| CA 2400797  | AA   | 20010830 | CA 2001-2400797 | 20010220   |
| AU 2001052135   | A5   | 20010903 | AU 2001-52135   | 20010220   |
| EP 1259292  | A2   | 20021127 | EP 2001-925343  | 20010220   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                 |            |
| JP 2003523410   | T2   | 20030803 | JP 2001-561399  | 20010220   |
| US 2003130355   | A1   | 20030710 | US 2002-204392  | 20021112   |
| PRIORITY APPLN. INFO.:  |      |          | GB 2000-4003    | A 20000222 |
|   |      |          | WO 2001-EP1894  | W 20010220 |

L9 ANSWER 56 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB A composition comprising: (a) a pharmaceutically effective amount of one or more norepinephrine reuptake inhibitors or a pharmaceutically effective salt thereof; and (b) a pharmaceutically effective amount of one or more antimuscarinic agents or a pharmaceutically effective salt thereof is provided. The composition is useful in treating disorders or diseases of the central nervous system, and particularly useful in treating incontinence. A composition was prepared containing reboxetine in either its racemic or enantiomer forms with tolterodine.

ACCESSION NUMBER: 2001:635879 CAPLUS  
 DOCUMENT NUMBER: 135:200472  
 TITLE: Norepinephrine reuptake inhibitor and antimuscarinic agent combinations  
 INVENTOR(S): Rogosky, Karen; Jorn, Deborah  
 PATENT ASSIGNEE(S): Pharmacia & Upjohn Co., USA  
 SOURCE: PCT Int. Appl., 21 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2001062236   | A2   | 20010830 | WO 2001-US3698  | 20010123   |
| WO 2001062236   | A3   | 20020307 |                 |            |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM |      |          |                 |            |
| RW: CH, GM, KE, LS, MW, MZ, SD, SL, SZ, TT, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| EP 1257277  | A2   | 20021120 | EP 2001-910421  | 20010123   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                 |            |
| JP 2003523382   | T2   | 20030805 | JP 2001-561303  | 20010123   |
| NZ 520975   | A    | 20040326 | NZ 2001-520975  | 20010123   |
| CA 2399442  | A2   | 20010830 | CA 2001-2399442 | 20010223   |
| AU 2001038028   | A5   | 20010903 | AU 2001-38028   | 20010223   |
| US 2002010216   | A1   | 20020124 | US 2001-792718  | 20010223   |
| PRIORITY APPLN. INFO.:  |      |          | US 2000-184790P | P 20000224 |
|   |      |          | WO 2001-US3698  | W 20010123 |

L9 ANSWER 58 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB ArCH(OAr1)CH2CH2NMeG [Ar = Ph, 2-thienyl; Ar1 = 1-naphthyl, 2-methoxyphenyl, 2-(methylthio)phenyl, 2-methylphenyl; G = H, Me] are prepared by reaction of the alkoxides of ArCH(OH)CH2CH2NMeG with Ar1X (X = F, Cl) in 1,3-dimethyl-2-imidazolidinone or N-methyl-2-pyrrolidinone as solvent. Thus, 10 g 3-hydroxy-N-methyl-3-phenylpropylamine and 7.5 g K tert-butoxide are heated with 20 mL 2-fluorotoluene in 25 mL 1,3-dimethyl-2-imidazolidinone at 110° for 20 h to give N-methyl-3-(2-methylphenoxyl)-3-phenylpropylamine, which was combined with (S)-(+)-mandelic acid in order to isolate the R isomer (as the hydrochloride) after decomposition of the salt.

ACCESSION NUMBER: 2000:742056 CAPLUS  
 DOCUMENT NUMBER: 133:296273  
 TITLE: Methods for preparing 3-aryloxy-3-arylpropylamines and their intermediates  
 INVENTOR(S): Kjell, Douglas Patton; Lorenz, Kurt Thomas  
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
 SOURCE: PCT Int. Appl., 25 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 2000061540   | A1   | 20000109 | WO 2000-US6423  | 20000322   |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM |      |          |                 |            |
| RW: CH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| CA 2362185  | AA   | 20000109 | CA 2000-2362185 | 20000322   |
| EP 1171417  | A1   | 20020116 | EP 2000-917868  | 20000322   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI   |      |          |                 |            |
| JP 2002541235   | T2   | 20020123 | JP 2000-610817  | 20000322   |
| US 6541668  | B1   | 20030401 | US 2001-936468  | 20010912   |
| PRIORITY APPLN. INFO.:  |      |          | US 1999-128480P | P 19990409 |
|   |      |          | WO 2000-US6423  | W 20000322 |

OTHER SOURCE(S): MARPAT 133:296273  
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

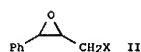
L9 ANSWER 57 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Preferential delivery via electrotransport of a preferred isomeric form of a pharmaceutically active chiral compound from a mixture of the isomeric forms of said compound is provided. A method of decreasing the delivery via electrotransport of a less preferred isomer of a drug is also provided. Following electrotransport administration of ketorolac, the mean amount of R isomer absorbed was lower than that of the S isomer.

ACCESSION NUMBER: 2000:754414 CAPLUS  
 DOCUMENT NUMBER: 133:325631  
 TITLE: Stereospecific delivery of a drug using electrotransport  
 INVENTOR(S): Gupta, Suneel K.; Sathyan, Gayatri; Padmanabhan, Rama  
 PATENT ASSIGNEE(S): ALZA Corporation, USA  
 SOURCE: U.S., 22 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE       |
|------------------------|------|----------|-----------------|------------|
| US 6136327             | A    | 20001024 | US 1997-982245  | 19971201   |
| JP 2000154364          | T2   | 20011204 | JP 2000-522969  | 19981130   |
| PRIORITY APPLN. INFO.: |      |          | US 1997-982245  | A 19971201 |
|                        |      |          | WO 1998-US25387 | W 19981130 |

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 59 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 GI



AB (S)-oxetane enantiomers such as tomoxetine, fluoxetine, and nisoxetine, which are serotonergic appetite depressants, represented by formula PhCH(OY)CH2CH2NR1R2 (I; R1 = H, C1-5 alkyl; R2 = C1-5 alkyl; Y = 4-trifluoromethylphenyl, 2-methylphenyl, 2-ethoxyphenyl; X = halo, HO, ester, amino) are prepared by method 1 involving steps (a) conversion of propiophenone represented by formula PhCOCH2CH2X (X = same as above) into racemic alcs. represented by formula PhCH(OH)CH2CH2X, under nonchiral conditions and (b) optical resolution of the latter racemic alcs. to (R)- and (S)-enantiomer with at least 95% enantiomeric purity by pseudo-moving bed chromatog. separation using chiral adsorbent and conversion of the (S)-alc. enantiomer into (S)-I or method 2 involving steps (a) selective conversion of 3-substituted 1-phenyl-1-propene represented by formula PhCH:CHCH2X (X = same as above) into racemic epoxides (II; X = same as above) under nonchiral conditions and conversion of the racemic epoxides into racemic or (b) optical resolution of the latter racemic epoxides to (R)- and (S)-enantiomer with at least 95% enantiomeric purity by pseudo-moving bed chromatog. separation using chiral adsorbent and conversion of the (S)-epoxide enantiomer into (S)-I. Undesired (R)-alc. and (R)-epoxide enantiomers are racemized and recycled to the optical resolution steps in methods 1 and 2.

In this process, racemic precursors undergo optical resolution with high optical purity at the early stage of the oxetane synthesis and the purity of the precursors is maintained and carried over to the products.

ACCESSION NUMBER: 2000:731520 CAPLUS  
 DOCUMENT NUMBER: 133:296272  
 TITLE: Method for preparation of (S)-oxetane enantiomers  
 INVENTOR(S): Gattuso, Marion J.  
 PATENT ASSIGNEE(S): UOP Inc., USA  
 SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.  
 CODEN: JKKXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO.   | DATE     |
|------------------------|------|----------|-------------------|----------|
| JP 2000290239          | A2   | 20001017 | JP 1999-87304     | 19990329 |
| PRIORITY APPLN. INFO.: |      |          | JP 1999-87304     | 19990329 |
| OTHER SOURCE(S):       |      |          | MARPAT 133:296272 |          |

L9 ANSWER 60 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB The discriminative stimulus (DS) effects of 4-aminopyridine (4-AP) were evaluated in 36 male Sprague-Dawley rats that were trained to discriminate

4-AP from saline in a standard two-lever food reinforced drug discrimination procedure. 4-AP along with its structural analogs 3-aminopyridine (3-AP),

2-aminopyridine (2-AP), and 2,3-diaminopyridine (2,3-DIAP) produced dose-dependent increases in the percentage of responses on the 4-AP-associated lever with full substitution at one or more doses.

2,6-Diaminopyridine (2,6-DIAP) and 3,4-diaminopyridine (3,4-DIAP) produced

dose-dependent increases in the percentage of responses on the 4-AP-associated lever but only partially substituted for 4-AP. Neither 4-dimethylaminopyridine (4-DMAP) nor pyridine substituted for 4-AP. Substitution studies were also conducted with indirect dopamine, norepinephrine, serotonin, and acetylcholine agonists, and  $\gamma$ -aminobutyric acid A (GABA) agonists and antagonists. The norepinephrine re-uptake inhibitor tomoxetine, but not nisoxetine or imipramine, produced dose-dependent increases in the percentage of responses on the 4-AP-associated lever and partially substituted for 4-AP.

In addition, antagonism studies were conducted using indirect dopamine, norepinephrine, serotonin, acetylcholine antagonists, and GABA agonists as pretreatments to the training dose of 4-AP. The benzodiazepine agonists chlordiazepoxide and diazepam dose dependently attenuated the DS effects of 4-AP. The present results demonstrate that the K-channel blocker 4-AP can be trained as a DS in rats and the DS effects of 4-AP are

likely mediated through blockade of voltage-dependent K-channels. The results also demonstrate a novel interaction between benzodiazepines and K-channels.

ACCESSION NUMBER: 2000:728414 CAPLUS  
DOCUMENT NUMBER: 134:13205  
TITLE: Pharmacological characterization of the discriminative stimulus effects of the potassium channel blocker 4-aminopyridine in rats  
AUTHOR(S): Brandsgaard, Roxanne; Barrett, James E.; Rosenzweig-Lipson, Sharon  
CORPORATE SOURCE: Wyeth-Ayerst Research, Princeton, NJ, USA  
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 295(1), 382-391  
CODEN: JPETAB; ISSN: 0022-3565  
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 61 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB This invention relates to the use of a CYP2D6 inhibitor in combination with a drug having CYP2D6-catalyzed metabolism, wherein the drug and the CYP2D6 inhibitor are not the same compound; and pharmaceutical compns.

for said use.  
ACCESSION NUMBER: 2000:725447 CAPLUS  
DOCUMENT NUMBER: 133:301178  
TITLE: Use of CYP2D6 inhibitors in combination therapies  
INVENTOR(S): Obach, Ronald Scott  
PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
SOURCE: PCT Int. Appl., 18 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE        |
|---|------|----------|-----------------|-------------|
| WO 2000059486   | A2   | 20001012 | WO 2000-1B304   | 20000320    |
| WO 2000059486   | C1   | 20020725 |                 |             |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |             |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |             |
| CA 2367052  | AA   | 20001012 | CA 2000-2367052 | 20000320    |
| BR 2000009564   | A    | 20020108 | BR 2000-9564    | 20000320    |
| EP 1242058  | A1   | 20020925 | EP 2000-909570  | 20000320    |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL   |      |          |                 |             |
| EE 200100524  | A    | 20021216 | EE 2001-524     | 20000320    |
| JP 2003523936   | T2   | 20030812 | JP 2000-609050  | 20000320    |
| AU 774923   | B2   | 20040715 | AU 2000-31850   | 20000320    |
| NZ 514466   | A    | 20041029 | NZ 2000-514466  | 20000320    |
| US 2003144220   | A1   | 20030731 | US 2000-528978  | 20000321    |
| HR 2001000722   | A1   | 20020831 | HR 2001-722     | 20011004    |
| ZA 2001008158   | A    | 20030724 | ZA 2001-8158    | 20011004    |
| NO 2001004858   | A    | 20011205 | NO 2001-4858    | 20011005    |
| BG 106075   | A    | 20020628 | BG 2001-106075  | 20011101    |
| US 2004018253   | A1   | 20040129 | US 2003-622301  | 20030718    |
| US 2004028755   | A1   | 20040212 | US 2003-624123  | 20030721    |
| PRIORITY APPLN. INFO.:  |      |          | US 1999-128136P | P 19990407  |
|   |      |          | WO 2000-1B304   | W 20000320  |
|   |      |          | US 2000-528978  | A3 20000321 |

L9 ANSWER 62 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB The title processes comprises stereoselective etherification of an alkoxide (sic) of (R)-PhCH(OR)CH<sub>2</sub>CH<sub>2</sub>NMe<sub>2</sub> (I; R = H) by 2-XC<sub>6</sub>H<sub>4</sub>Z1 (X = halo, Z1 = e.g., CH(OR1)OR11 or CH<sub>2</sub>NR2; R1, R11 = alkyl or CH<sub>2</sub>Ph; R1R11 = alkylene; R2 = alkyl or (un)substituted Ph) to give I (R = C<sub>6</sub>H<sub>4</sub>Z1-2) followed by conversion of Z1 to Me.

ACCESSION NUMBER: 2000:707122 CAPLUS  
DOCUMENT NUMBER: 133:281603  
TITLE: Preparation of tomoxetine  
INVENTOR(S): Heath, Perry Clark; Ratz, Andrew Michael; Weigel, Leland Otto  
PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
SOURCE: PCT Int. Appl., 59 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE       |
|---|------|----------|---|------------|
| WO 2000058262   | A1   | 20001005 | WO 2000-US2527  | 20000229   |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |   |            |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |   |            |
| PRIORITY APPLN. INFO.:  |      |          | US 1999-126701P   | P 19990329 |
| OTHER SOURCE(S):  |      |          | CASREACT 133:281603; MARPAT 133:281603  |            |
| REFERENCE COUNT:  |      |          | 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE |            |
| FORMAT  |      |          |   |            |

L9 ANSWER 63 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB The locus coeruleus (LC) is the largest norepinephrine cell group in the central nervous system and contains a high d. of norepinephrine (NE) uptake sites. Alc.-preferring (AP) rats and high-alc.-drinking (HAD) rats are selectively bred for high alc. preference, whereas alc.-nonpreferring (NP) rats and low-alc.-drinking (LAD) rats are bred for low alc. preference. However, it is unknown whether NE uptake sites in the LC are associated with alc. preference in AP and HAD rats when compared with their resp. control rats, NP and LAD rats. This study was designed to examine this question. Animals were decapitated and brains were removed, frozen with dry ice powder, and stored in a deep freezer. The LC tissue blocks were cut into 14 µ cryostat sections, collected on glass slides, and incubated with 0.6 nM [3H]-tomoxetine in 50 mM Tris-HCl buffer system. For nonspecific binding, 1 µM desipramine was added to the radioactive ligand. Sections were rinsed, quickly dried, and processed for quant. autoradiog. In addition, galanin content in the LC was also studied.

The LC possessed a high d. of [3H]-tomoxetine binding sites. There were fewer tomoxetine binding sites (fmol/mg protein) in the AP rats (433.0 ± 8.1) than in the NP rats (495.6 ± 3.7). HAD rats (386.5 ± 13.2) also possessed fewer tomoxetine binding sites than LAD rats (458.7 ± 10.1). Galanin content in the LC was similar between AP and NP rats and between HAD and LAD rats. Because both AP rats and HAD rats were selectively bred for alc. preference, the finding of consistently low levels of [3H]-tomoxetine binding in the LC of these two lines of rats with high alc. preference suggests that down-regulation of NE transporters in the LC of AP and HAD rats may be associated with alc.-seeking behavior. A possible involvement of the coerulear NE uptake sites in depression is also discussed. Galanin in the LC may not relate to alc. preference.

ACCESSION NUMBER: 2000:415187 CAPLUS  
 DOCUMENT NUMBER: 133:173275  
 TITLE: Norepinephrine uptake sites in the locus coeruleus of rat lines selectively bred for high and low alcohol preference: a quantitative autoradiographic binding study using [3H]-tomoxetine  
 AUTHOR(S): Hwang, Bang H.; Wang, Guo-Ming; Wong, David T.; Lumeng, Lawrence; Li, T.-K.  
 CORPORATE SOURCE: Department of Anatomy, School of Medicine, Indiana University, Indianapolis, IN, USA  
 SOURCE: Alcoholism: Clinical and Experimental Research (2000), 24(5), 588-594  
 CODEN: ACRSDM; ISSN: 0145-6008  
 PUBLISHER: Lippincott Williams & Wilkins  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 64 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB 3-Chloro-1-phenylpropan-1-ol and the corresponding butanoate, 3-chloro-1-phenylpropyl butanoate, were kinetically resolved using lipase B from *Candida antarctica* catalysis by transesterification and hydrolysis resp. The resulting chiral building blocks, (S)- and (R)-3-chloro-1-phenylpropanol, were converted into both enantiomers of the antidepressant drugs Fluoxetine, Tomoxetine and Nisoxetine.

ACCESSION NUMBER: 2000:361406 CAPLUS  
 DOCUMENT NUMBER: 133:237610  
 TITLE: Chemoenzymatic synthesis of the non-tricyclic antidepressants Fluoxetine, Tomoxetine and Nisoxetine  
 AUTHOR(S): Liu, Hui-Ling; Hoff, Bard Helge; Anthonson, Thorleif  
 CORPORATE SOURCE: Department of Chemistry, Norwegian University of Science and Technology, Trondheim, N-7491, Norway  
 SOURCE: Perkin 1 (2000), (11), 1767-1769  
 CODEN: PERKF9  
 PUBLISHER: Royal Society of Chemistry  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 133:237610  
 REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 65 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Pharmaceutical compds. which comprise R(-) fluoxetine and one or more other biol. active compds. e.g. a benzodiazepine compound, a tricyclic antidepressant, a 5-HT1A receptor antagonist, a 5-HT3 receptor agonist, a β-adrenergic antagonist, an antipsychotic agent, an anti-anxiolytic or other psychotropic drug, are disclosed. Methods of treating or preventing a disease or disorder, especially a psychotic or psychiatric disease or disorder, using the above pharmaceutical composition or by administering a R(-) fluoxetine in combination with one or more other biol. active compds. are also disclosed. Methods of treating patients having or at risk of having AIDS or HIV infection, cancer, cardiac disorder, post-myocardial depression and post-traumatic stress disorder using optically pure R(-) fluoxetine in combination with one or more other biol. active compds. are further disclosed.

ACCESSION NUMBER: 1999:763863 CAPLUS  
 DOCUMENT NUMBER: 132:6368  
 TITLE: Compositions and methods employing R(-) fluoxetine and other active ingredients  
 INVENTOR(S): Barberich, Timothy J.; Rubin, Paul D.; Handley, Dean A.  
 PATENT ASSIGNEE(S): Sepracor Inc., USA  
 SOURCE: PCT Int. Appl., 41 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO. | DATE        |
|------------------------|--|----------|-----------------|-------------|
| WO 9961014             | A2   | 19991202 | WO 1999-US11725 | 19990527    |
| WO 9961014             | A3   | 20000720 |                 |             |
| W:                     | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |             |
| RW:                    | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG   |          |                 |             |
| AU 9941006             | A1   | 19991213 | AU 1999-41006   | 19990527    |
| US 2002151543          | A1   | 20021017 | US 2002-158886  | 20020603    |
| PRIORITY APPLN. INFO.: |  |          | US 1998-86262   | A 19980528  |
|                        |  |          | US 1998-177703  | B2 19981023 |
|                        |  |          | WO 1999-US11725 | W 19990527  |
|                        |  |          | US 2000-664732  | B3 20000919 |

L9 ANSWER 66 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB A review with 52 refs. Lilly is developing tomoxetine, a norepinephrine uptake inhibitor, for the potential treatment of attention deficit hyperactivity disorder (ADHD) and depression. The drug is undergoing phase II clin. testing in 7 to 13-yr old patients with attention deficit disorders [275533], [326984]. In a randomized placebo-controlled phase II study in adults with childhood-onset and persistent ADHD, tomoxetine (40 mg/day increasing to 80 mg/day for 3 wk) reduced symptoms measured on the ADHD rating scale [326909]. Tomoxetine was first investigated by Lilly in the 1980s as a potential treatment for depressive illness. The compound was selected from a series of potent inhibitors of norepinephrine reuptake, and reached phase II clin. trials for depression in 1990. Development appeared to stop at that time, in spite of some evidence that tomoxetine was fairly effective [273943]. In 1996, Lilly apparently restarted preclin. development of tomoxetine as a potential therapy for ADHD, and submitted EP-00721777 claiming tomoxetine's utility for this disorder in July of that year [273956]. In Feb. 1999, Deutsche Bank predicted sales of \$100 million in 2001 rising to \$400 million in 2003 [316821].

ACCESSION NUMBER: 1999:661307 CAPLUS  
 DOCUMENT NUMBER: 131:266451  
 TITLE: Tomoxetine (Eli Lilly)  
 AUTHOR(S): Preti, Antonio  
 CORPORATE SOURCE: Psychiatry Branch, Genneruxi Medical Center, Cagliari, 09129, Italy  
 SOURCE: Current Opinion in Central & Peripheral Nervous System  
 Investigational Drugs (1999), 1(4), 514-520  
 CODEN: COCDFA; ISSN: 1464-844X  
 PUBLISHER: Current Drugs Ltd.  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English  
 REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 67 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB A method for producing a potentiating effect on a therapeutic action of an agent which is selected from a serotonin re-uptake inhibitor, a norepinephrine re-uptake inhibitors, both a serotonin and norepinephrine re-uptake inhibitor, and an atypical antidepressant in a warm blooded mammal, comprises administering to said mammal an effective amount of moxonidine, or a pharmaceutically acceptable salt thereof. A tablet contained moxonidine 0.300, lactose 95.700, povidone 0.700, crospovidone 3.000, magnesium stearate 0.300, hydroxypropyl Me cellulose 1.300, Et cellulose 1.200, PEG 0.250, talc 0.975, red ferric oxide 0.025, and titanium dioxide 1.250 mg. Moxonidine at 0.2 mg twice daily when combined with 20 mg fluoxetine daily had synergistic effects in patients suffering major depression.

ACCESSION NUMBER: 1999:282100 CAPLUS  
 DOCUMENT NUMBER: 130:316651  
 TITLE: Synergistic pharmaceutical compositions containing moxonidine  
 INVENTOR(S): Perry, Kenneth Wayne  
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
 SOURCE: PCT Int. Appl., 27 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| WO 9920279  | A1   | 19990429 | WO 1998-US21418 | 19981009   |
| W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |            |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| CA 2306233  | AA   | 19990429 | CA 1998-2306233 | 19981009   |
| AU 9896928  | A1   | 19990510 | AU 1998-96928   | 19981009   |
| EP 919234   | A2   | 19990602 | EP 1998-308225  | 19981009   |
| EP 919234   | A3   | 19990825 |                 |            |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |      |          |                 |            |
| ZA 9809251  | A    | 20000410 | ZA 1998-9251    | 19981009   |
| US 6066643  | A    | 20000523 | US 1998-169369  | 19981009   |
| JP 2001520195   | T2   | 20011030 | JP 2000-516676  | 19981009   |
| PRIORITY APPLN. INFO.:  |      |          | US 1997-62282P  | P 19971017 |
|   |      |          | WO 1998-US21418 | W 19981009 |

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 69 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Norepinephrine reuptake inhibitors (e.g. duloxetine) are used to treat oppositional defiant disorder.

ACCESSION NUMBER: 1999:231508 CAPLUS  
 DOCUMENT NUMBER: 130:262137  
 TITLE: Norepinephrine reuptake inhibitor for treatment of oppositional defiant disorder  
 INVENTOR(S): Heiligenstein, John Harrison  
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
 SOURCE: PCT Int. Appl., 15 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE       |
|---|------|----------|-------------------|------------|
| WO 9915176  | A1   | 19990401 | WO 1998-US18114   | 19980901   |
| W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                   |            |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                   |            |
| CA 2304115  | AA   | 19990401 | CA 1998-2304115   | 19980901   |
| AU 9891282  | A1   | 19990412 | AU 1998-91282     | 19980901   |
| AU 740109   | B2   | 20011101 |                   |            |
| BR 9812357  | A    | 20000912 | BR 1998-12357     | 19980901   |
| TR 200000755  | T2   | 20000921 | TR 2000-200000755 | 19980901   |
| JP 2001517627   | T2   | 20011009 | JP 2000-512545    | 19980901   |
| NZ 502810   | A    | 20002031 | NZ 1998-502810    | 19980901   |
| US 6028070  | A    | 20000222 | US 1998-156289    | 19980917   |
| EP 919236   | A1   | 19990602 | EP 1998-307650    | 19980921   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |      |          |                   |            |
| NO 2000001458   | A    | 20000321 | NO 2000-1458      | 20000321   |
| PRIORITY APPLN. INFO.:  |      |          | US 1997-59629P    | P 19970923 |
|   |      |          | WO 1998-US18114   | W 19980901 |

OTHER SOURCE(S): MARPAT 130:262137  
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 68 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB A simple, systematic method was developed for rapidly screening potential capillary electrophoresis (CE) separation conditions for small, amine-containing enantiomers. During method development, 39 pairs of enantiomers were studied and partial or complete separation was achieved in every case. Baseline resolution was achieved by these initial screening conditions in over half of the cases. The screening strategy uses a bare fused silica capillary and a pH 2.5 amine-modified phosphate buffer containing one of the selected cyclodextrins (CD): dimethyl-β-CD, hydroxypropyl-β-CD, hydroxypropyl-α-CD, hydroxypropyl-γ-CD and sulfated-β-CD. An addnl. set of compds. were screened by this approach to demonstrate the validity of the method. The paper outlines the exptl. work carried out to develop the screen and describes how one might implement it for a new compound

ACCESSION NUMBER: 1999:244205 CAPLUS  
 DOCUMENT NUMBER: 130:346558  
 TITLE: Systematic screening approach for chiral separations of basic compounds by capillary electrophoresis with modified cyclodextrins  
 AUTHOR(S): Liu, Li; Nussbaum, Mark A.  
 CORPORATE SOURCE: Pharmaceutical Sciences Division, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA  
 SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1999), 19(5), 679-694  
 CODEN: JPBADA; ISSN: 0731-7085  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 70 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Norepinephrine reuptake inhibitors (e.g. duloxetine) are used to treat conduct disorder.

ACCESSION NUMBER: 1999:231496 CAPLUS  
 DOCUMENT NUMBER: 130:262136  
 TITLE: Norepinephrine reuptake inhibitors for treatment of conduct disorder  
 INVENTOR(S): Heiligenstein, John Harrison  
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
 SOURCE: PCT Int. Appl., 18 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO.   | DATE       |
|---|------|----------|-------------------|------------|
| WO 9915163  | A1   | 19990401 | WO 1998-US18103   | 19980901   |
| W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                   |            |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                   |            |
| CA 2304657  | AA   | 19990401 | CA 1998-2304657   | 19980901   |
| AU 9890417  | A1   | 19990412 | AU 1998-90417     | 19980901   |
| AU 740192   | B2   | 20011101 |                   |            |
| BR 9812371  | A    | 20000919 | BR 1998-12371     | 19980901   |
| TR 200000756  | T2   | 20000921 | TR 2000-200000756 | 19980901   |
| JP 2001517619   | T2   | 20011009 | JP 2000-512532    | 19980901   |
| NZ 502853   | A    | 20002028 | NZ 1998-502853    | 19980901   |
| US 6184222  | B1   | 20010206 | US 1998-156285    | 19980917   |
| EP 919235   | A1   | 19990602 | EP 1998-307630    | 19980921   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |      |          |                   |            |
| NO 2000001479   | A    | 20000322 | NO 2000-1479      | 20000322   |
| PRIORITY APPLN. INFO.:  |      |          | US 1997-59628P    | P 19970923 |
|   |      |          | WO 1998-US18103   | W 19980901 |

OTHER SOURCE(S): MARPAT 130:262136  
 REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT



L9 ANSWER 71 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB In an effort to identify novel binding sites for cocaine and its analogs, the authors carried out binding studies with the high-affinity and selective ligand [125I]RTI-121 in rat frontal cortical tissue. Very low densities of binding sites were found. Saturation anal. revealed that the binding was to both high- and low-affinity sites. Pharmacol. competition studies were carried out with inhibitors of the dopamine, norepinephrine, and serotonin transporters. The various transporter inhibitors inhibited the binding of 15 pM [125I]RTI-121 in a biphasic fashion following a two-site binding model. The resultant data were complex and did not suggest a simple association with any single transporter. Correlational anal. supported the following hypothesis: [125I] RTI-121 binds to known transporters and not to novel sites; these include dopamine, norepinephrine, and serotonin transporters. Immunopptn. of transporters photoaffinity labeled with [125I]RTI-82 and subsequent anal. of SDS-page gels revealed the presence of authentic dopamine transporters in these samples; displacement of the photoaffinity label occurred with a typical dopamine transporter pharmacol. These data are compatible with the binding properties of RTI-121 and the presence of several known transporters in the tissue studied.

ACCESSION NUMBER: 1998:506893 CAPLUS  
 DOCUMENT NUMBER: 129:225624  
 TITLE: Multiple binding sites for [125I]RTI-121 and other cocaine analogs in rat frontal cerebral cortex  
 AUTHOR(S): Boja, J. W.; Carroll, F. I.; Vaughan, R. A.; Kopajtich, T.; Kuhar, M. J.  
 CORPORATE SOURCE: Dept. of Pharmacology, N.E. Ohio Universities College of Medicine, Rootstown, OH, 44266, USA  
 SOURCE: Synapse (New York) (1998), 30(1), 9-17  
 CODEN: SYNACT; ISSN: 0887-4476  
 PUBLISHER: Wiley-Liss, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 73 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Using radioligand binding assays, we determined the equilibrium dissociation constants (K<sub>D</sub>'s) for 37 antidepressants, three of their metabolites (desmethylcitalopram, desmethylsertraline, and norfluoxetine), some mood stabilizers, and assorted other compounds. (some antiepileptics, Ca<sup>2+</sup> channel antagonists, benzodiazepines, psychostimulants, antihistamines, and monoamines) for the human serotonin, norepinephrine, and dopamine transporters. Among the compounds that we tested, mazindol was the most potent at the human norepinephrine and dopamine transporters with K<sub>D</sub>'s of 0.45±0.03 nM and 8.1±0.4 nM, resp. Sertraline (K<sub>D</sub>=25±2 nM) and nomifensine (56±3 nM) were the two most potent antidepressants at the human dopamine transporter. We showed significant correlations for antidepressant affinities at binding to serotonin (R=0.93), norepinephrine (R=0.97), and dopamine (R=0.87) transporters in comparison to their resp. values for inhibiting uptake of monoamines into rat brain synaptosomes. These data are useful in predicting some possible adverse effects and drug-drug interactions of antidepressants and related compounds.

ACCESSION NUMBER: 1997:808034 CAPLUS  
 DOCUMENT NUMBER: 128:149531  
 TITLE: Pharmacological profile of antidepressants and related compounds at human monoamine transporters  
 AUTHOR(S): Tatsumi, Masahiko; Groshan, Karen; Blakely, Randy D.; Richelson, Elliott  
 CORPORATE SOURCE: San Pablo Road, Mayo Clinic Jacksonville, Jacksonville, FL 32224, 4500, USA  
 SOURCE: European Journal of Pharmacology (1997), 340(2/3), 249-258  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 72 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Cocaine, which non-selectively blocks the reuptake of the monoamines serotonin, dopamine and norepinephrine, produces weak antinociceptive effects and increases the antinociceptive effects of low- to intermediate-efficacy mu opioid agonists in rhesus monkeys. In the present study, the antinociceptive effects of more selective monoamine reuptake inhibitors administered alone and in combination with mu opioid agonists were evaluated in rhesus monkeys using a warm-water tail-withdrawal assay of thermal nociception. Like cocaine, the selective serotonin reuptake inhibitors clomipramine (0.01-3.2 mg/kg) and fluoxetine (0.1-10 mg/kg) produced weak antinociceptive effects. Pretreatment with the serotonin receptor antagonist mianserin (0.032-0.32 mg/kg) produced rightward and downward shifts in the clomipramine dose-effect curve, suggesting that the effects of clomipramine were mediated by serotonin receptors. Combination of clomipramine with the low efficacy mu agonist nalbuphine or the intermediate efficacy mu agonist morphine produced more antinociception than did the mu agonists alone. Fluoxetine also produced a small leftward shift in the morphine dose-effect curve. The selective norepinephrine reuptake inhibitors nisoxetine (0.1-10 mg/kg) and tomoxetine (0.1-10 mg/kg) and the selective dopamine reuptake inhibitors bupropion (0.032-3.2 mg/kg) and GBR 12909 (0.1-10 mg/kg) did not produce antinociception or increase antinociception induced by nalbuphine or morphine. In fact, GBR 12909 produced dose-dependent allodynia and reduced the maximal antinociceptive effects of morphine. These results suggest that inhibition of serotonin reuptake is sufficient to produce weak antinociceptive effects and enhance the antinociceptive effects of low efficacy mu opioid agonists. These results also suggest that the effects of cocaine on serotonin reuptake may contribute to cocaine's antinociceptive effects in rhesus monkeys.

ACCESSION NUMBER: 1998:94039 CAPLUS  
 DOCUMENT NUMBER: 128:226105  
 TITLE: Antinociceptive effects of monoamine reuptake inhibitors administered alone or in combination with mu opioid agonists in rhesus monkeys  
 AUTHOR(S): Gatch, Michael B.; Negus, S. Stevens; Mello, Nancy K.  
 CORPORATE SOURCE: Alcohol and Drug Abuse Research Center, McLean Hospital-Harvard Medical School, Belmont, MA, 02178, USA  
 SOURCE: Psychopharmacology (Berlin) (1998), 135(1), 99-106  
 CODEN: PSCHDL; ISSN: 0033-3158  
 PUBLISHER: Springer-Verlag  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 74 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB It has been demonstrated that castration alters the functioning of the olfactory bulb (OB)-norepinephrine (NE) system. In the present experiment, we examined one of the mechanisms by which castration modulates the OB-NE system by comparing NE uptake activity between intact and castrated male rats as studied using an in vitro superfusion technique. To accomplish this goal, NE output from the OB of intact and castrated male rats in response to infusion with two different drugs which alter NE uptake functions, tomoxetine and talsupram, were tested. Overall, NE outputs in response to tomoxetine were significantly higher in the castrated than in intact rats and both groups were significantly greater than non-infused controls. For the talsupram infusion group, NE outputs from the castrated, but not intact rats, were significantly greater than controls. No statistically significant differences were detected between the castrated and intact rats. These results demonstrate that castration alters the NE uptake activities in response to these noradrenergic uptake blockers and suggest that one mechanism by which castration alters OB-NE functioning is through reducing the uptake activity of NE within the OB. Such findings have important implications for olfactory-based learning and memory/recognition processes which are believed to involve the OB-NE system and are altered following castration.

ACCESSION NUMBER: 1997:795642 CAPLUS  
 DOCUMENT NUMBER: 128:97995  
 TITLE: Castration reduces olfactory bulb norepinephrine transporter function as indicated by responses to noradrenergic uptake blockers  
 AUTHOR(S): Shang, Yili; Dluzen, Dean E.  
 CORPORATE SOURCE: State Route 44, P.O. Box 95, Department of Anatomy, Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272-0095, 4209, USA  
 SOURCE: Brain Research (1998), 779(1,2), 119-124  
 CODEN: BRREAP; ISSN: 0006-8993  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L9 ANSWER 75 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Exhaustive conformational analyses on four selective serotonin reuptake inhibitors resulted in a pharmacophoric model explaining observed differences in enantioselectivities. A number of test compds. from a diverse set of chemical structures was included in the evaluation of the model. Furthermore, selectivity towards noradrenaline reuptake is explained.

ACCESSION NUMBER: 1997:545611 CAPLUS  
 DOCUMENT NUMBER: 127:199618  
 TITLE: A stereoselective pharmacophoric model of the serotonin re-uptake site  
 AUTHOR(S): Gundertofte, Klaus; Bogeso, Klaus P.; Liljefors, Tommy  
 CORPORATE SOURCE: Research and Development, Copenhagen, DK-2500, Den.  
 SOURCE: Computer-Assisted Lead Finding and Optimization: Current Tools for Medicinal Chemistry, [European Symposium on Quantitative Structure-Activity Relationships], 11th, Lausanne, Sept. 1-6, 1996

(1997)

Meeting Date 1996, 445-459. Editor(s): Van de Waterbeemd, Han; Testa, Bernard; Folkers, Gerd.  
 Verlag Helvetica Chimica Acta: Basel, Switz.  
 CODEN: 64VEAH  
 CONFERENCE: Conference  
 LANGUAGE: English

L9 ANSWER 76 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The dissociation rates of [3H]nisoxetine, [3H]GBR 12935 and [3H]citalopram from, resp., the rat brain noradrenaline, dopamine and 5-HT transporters were found to be markedly affected by several drugs. Sertraline strongly attenuated the rate of dissociation of [3H]nisoxetine from the noradrenaline transporter, while citalopram strongly attenuated that of [3H]citalopram from the 5-HT transporter. The effects of both drugs were stereospecific. Less potent affinity-modulating drugs were identified with regards to [3H]GBR 12935 dissociation from the dopamine transporter. All three neuronal monoamine transporters may thus have specific affinity-modulating sites which change the function of the transporters with possible implications for the reuptake of monoamines released during synaptic activity.

ACCESSION NUMBER: 1997:272250 CAPLUS  
 DOCUMENT NUMBER: 126:339164  
 TITLE: An affinity-modulating site on neuronal monoamine transport proteins  
 AUTHOR(S): Plenge, Per; Møllerup, Erling T.  
 CORPORATE SOURCE: Laboratory of Neuropsychiatry, Department of Pharmacology, University of Copenhagen, Copenhagen, DK-2100, Den.  
 SOURCE: Pharmacology & Toxicology (Copenhagen) (1997), 80(4), 197-201  
 CODEN: PHTOEH; ISSN: 0901-9928  
 PUBLISHER: Munksgaard  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 77 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Tomoxetine, a norepinephrine uptake inhibitor, is used to treat attention-deficit/hyperactivity disorder.

ACCESSION NUMBER: 1996:483626 CAPLUS  
 DOCUMENT NUMBER: 125:132798  
 TITLE: Use of tomoxetine for the treatment of attention deficit-hyperactivity disorder  
 INVENTOR(S): Heiligenstein, John Harrison; Tollefson, Gary Dennis  
 PATENT ASSIGNEE(S): Eli Lilly and Co., USA  
 SOURCE: Eur. Pat. Appl., 4 pp.  
 CODEN: EPXNDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| EP 721777   | A2   | 19960717 | EP 1996-300157  | 19960109   |
| EP 721777   | A3   | 19970305 |                 |            |
| EP 721777   | B1   | 20020828 |                 |            |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE   |      |          |                 |            |
| US 5658590  | A    | 19970819 | US 1995-371341  | 19950111   |
| CA 2209735  | AA   | 19960718 | CA 1996-2209735 | 19960104   |
| CA 2209735  | C    | 20021001 |                 |            |
| WO 9621430  | A1   | 19960718 | WO 1996-US91    | 19960104   |
| W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ |      |          |                 |            |
| RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| AU 9646938  | A1   | 19960731 | AU 1996-46938   | 19960104   |
| AU 688665   | B2   | 19980312 |                 |            |
| BR 9606903  | A    | 19971021 | BR 1996-6903    | 19960104   |
| CN 1168095  | A    | 19971217 | CN 1996-191412  | 19960104   |
| JP 10512262   | T2   | 19981124 | JP 1996-521732  | 19960104   |
| NZ 301500   | A    | 20000728 | NZ 1996-301500  | 19960104   |
| RU 2163802  | C2   | 20010310 | RU 1997-113060  | 19960104   |
| RO 118374   | B1   | 20030530 | RO 1997-1260    | 19960104   |
| CZ 292226   | B6   | 20030813 | CZ 1997-2145    | 19960104   |
| PL 187573   | B1   | 20040831 | PL 1996-321273  | 19960104   |
| AT 222757   | E    | 20020915 | AT 1996-300157  | 19960109   |
| PT 721777   | T    | 20021129 | PT 1996-300157  | 19960109   |
| ES 2181845  | T3   | 20030301 | ES 1996-300157  | 19960109   |
| NO 9703170  | A    | 19970902 | NO 1997-3170    | 19970708   |
| FI 9702922  | A    | 19970709 | FI 1997-2922    | 19970709   |
| PRIORITY APPLN. INFO.:  |      |          | US 1995-371341  | A 19950111 |
|   |      |          | WO 1996-US91    | W 19960104 |

L9 ANSWER 78 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB (S)-1-Phenyl-3-buten-1-ol (1), prepared in high optical purity by enzymic resolution of the racemate, is a convenient building block for the synthesis of (R)-fluoxetine (7a) and (R)-tomoxetine (7b). Compound 1 was converted to the title drugs by etherification with appropriate phenols under Mitsunobu conditions, ozonolysis of the terminal double bond, mesylation of the resulting alc. and substitution with methylamine.

ACCESSION NUMBER: 1996:432302 CAPLUS  
 DOCUMENT NUMBER: 125:221272  
 TITLE: An efficient chemoenzymic route to the antidepressants (R)-fluoxetine and (R)-tomoxetine  
 AUTHOR(S): Bracher, Franz; Litz, Thomas  
 CORPORATE SOURCE: Institut für Pharmazeutische Chemie, Technischen Universität Braunschweig, Braunschweig, 38106, Germany  
 SOURCE: Bioorganic & Medicinal Chemistry (1996), 4(6), 877-880  
 CODEN: BMECEP; ISSN: 0968-0896  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 79 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB This experiment was designed to elucidate the neurotransmitter systems that mediate the discriminative stimulus effects of methamphetamine. Pigeons were trained to peck 1 key following saline injections and a 2nd key following methamphetamine injections (1.0 or 1.7 mg/kg, i.m.). Substitution tests revealed drug-appropriate responding following administration of the psychomotor stimulants methamphetamine, amphetamine and cocaine, the dopamine (DA) reuptake inhibitor bupropion, the norepinephrine (NE) reuptake inhibitors imipramine and tomoxetine, and the serotonin (5-HT) releaser fenfluramine. Saline-key responding occurred following administration of the D1 agonist SKF-38393, the D1 antagonist SCH-23390, the  $\alpha_2$ -receptor agonist clonidine, the  $\alpha_1$ -antagonist prazosin, the nonselective  $\beta$ -antagonist propranolol and the selective 5-HT reuptake inhibitor fluoxetine. The D2/D3 agonist quinpirole produced drug-appropriate responding in 2 pigeons and partial substitution in the remaining 2 pigeons. The 5HT1A agonist 8-OH-DPAT produced drug-appropriate responding at higher doses (0.3-1.0 mg/kg), whereas much lower doses (0.003-0.1 mg/kg) antagonized the methamphetamine stimulus. The stimulus effects of methamphetamine were attenuated by pretreatment with prazosin, SCH-23390 and eticlopride, whereas pretreatment with propranolol and the 5-HT3 antagonist MDL 72222 failed to attenuate reliably drug-induced key responding. These results suggest that NE and DA reuptake inhibition and 5-HT release mediate the discriminative stimulus effects of methamphetamine, as do the 5-HT1A and DA D1 and D2 receptors.

ACCESSION NUMBER: 1995:809369 CAPLUS  
 DOCUMENT NUMBER: 123:218304  
 TITLE: The discriminative stimulus effects of methamphetamine in pigeons  
 AUTHOR(S): Sasaki, J. E.; Tatham, T. A.; Barrett, J. E.  
 CORPORATE SOURCE: Dep. Psychiatry, Univ. Health Sci., Bethesda, MD, 20814, USA  
 SOURCE: Psychopharmacology (Berlin) (1995), 120(3), 303-10  
 CODEN: PSCHDL; ISSN: 0033-3158  
 PUBLISHER: Springer  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 81 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Thionisoxetine, a novel analog of the potent and selective norepinephrine (NE) uptake inhibitor nisoxetine, was evaluated. Thionisoxetine more potently inhibited the uptake of [3H]NE into rat hypothalamic synaptosomes and the binding of [3H]nisoxetine to the NE transporter than did (R)-nisoxetine. The (R) enantiomer of this compound was more potent than the (S) enantiomer, having a  $K_i$  of 0.20 nM in [3H]nisoxetine binding. The (R) enantiomer was approx. 70-fold more potent in inhibiting [3H]NE uptake than [3H]5HT uptake. In rats, (R)-thionisoxetine prevented hypothalamic NE depletion by 6-hydroxydopamine with an ED50 of 0.21 mg/kg. Depletion of NE in peripheral nerves was accomplished by the administration of metaraminol to rats. In this paradigm, (R)-thionisoxetine prevented the depletion of heart NE with an ED50 of 3.4 mg/kg and depletion of urethral NE with an ED50 of 1.2 mg/kg. Thus, (R)-thionisoxetine is a potent and selective inhibitor of NE uptake in both central and peripheral tissues.

ACCESSION NUMBER: 1995:521791 CAPLUS  
 DOCUMENT NUMBER: 122:282104  
 TITLE: (R)-Thionisoxetine, a potent and selective inhibitor of central and peripheral norepinephrine uptake  
 AUTHOR(S): Gehlert, Donald R.; Hemrick-Leucke, Susan K.; Douglas A.; Krushinski, Joseph; Howbert, J. Jeffry; Robertson, David W.; Wong, David T.; Fuller, Ray W.  
 CORPORATE SOURCE: Central Nervous System Res., Lilly Res. Lab., Div. E11  
 SOURCE: Life Sciences (1995), 56(22), 1915-20  
 CODEN: LIFSAR; ISSN: 0024-3205  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 80 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB (R)-[3H]tomoxetine is a radioligand that binds to the norepinephrine (NE) uptake site with high affinity but also binds to a second, lower-affinity site. The goal of the present study was to identify the nature of this low-affinity site by comparing the binding properties of (R)-[3H]tomoxetine with those of (R/S)-[3H]nisoxetine, a highly selective ligand for the NE uptake site. In homogenate binding studies, both radioligands bound to the NE uptake site with high affinity, whereas (R)-[3H]tomoxetine also bound to a second, lower-affinity site. The autoradiographic distribution of binding sites for both radioligands is consistent with the known distribution of NE-containing neurons. However, low levels of (R)-[3H]-tomoxetine binding were seen in the caudate-putamen, globus pallidus, olfactory tubercle, and zona reticulata of the substantia nigra, where (R/S)-[3H]nisoxetine binding was almost absent. In homogenates of the caudate-putamen, the NE uptake inhibitors desipramine and (R)-nisoxetine and the serotonin (5-HT) uptake inhibitor citalopram produced biphasic displacement curves. Autoradiographic studies using 10 nM (R)-nisoxetine to mask the binding of (R)-[3H]tomoxetine to the NE uptake site produced autoradiograms that were similar to those produced by [3H]citalopram. Therefore, (R)-[3H]tomoxetine binds to the NE uptake site with high affinity and the 5-HT uptake site with somewhat lower affinity.

ACCESSION NUMBER: 1995:579657 CAPLUS  
 DOCUMENT NUMBER: 122:306469  
 TITLE: Comparison of (R)-[3H]tomoxetine and (R/S)-[3H]nisoxetine binding in rat brain  
 AUTHOR(S): Gehlert, Donald R.; Schober, Douglas A.; Gackenhimer, Susan L.  
 CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, USA  
 SOURCE: Journal of Neurochemistry (1995), 64(6), 2792-800  
 CODEN: JONRA9; ISSN: 0022-3042  
 PUBLISHER: Lippincott-Raven  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 82 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Halogenated analogs of the potent norepinephrine (NE) uptake inhibitor, tomoxetine, were synthesized and their affinities for the serotonin (5HT) and NE uptake sites evaluated. One of the most potent was the 2-iodo substituted analog (289306) that inhibited [3H]tomoxetine binding to rat cerebral cortex with a  $K_i$  of 0.37 nM. The compound also inhibited the uptake of [3H]NE into rat hypothalamic synaptosomes with a  $K_i$  of 3.5 nM. This analog was significantly less potent at the 5HT uptake site, as exhibited by a  $K_i$  of 25 nM in the inhibition of [3H]paroxetine binding and a  $K_i$  of 121 nM in [3H]5HT uptake. The resolved (R) enantiomer (303926) was 10 times more potent as a [3H]NE uptake inhibitor and 29 times more potent as an inhibitor of [3H]tomoxetine binding than the (S) enantiomer (303884). Administration of 289306 to rats prior to an i.c.v. injection of 6-hydroxydopamine prevented the depletion of hypothalamic NE and Epi with ED50 values of 0.28 and 0.47 mg/kg, resp. Thus, 289306 was a potent inhibitor of NE uptake in vitro and in vivo. In addition, these compounds provide structures for potential ligands for the study of NE uptake sites by autoradiography, PET or SPECT imaging.

ACCESSION NUMBER: 1995:356183 CAPLUS  
 DOCUMENT NUMBER: 122:178224  
 TITLE: Novel halogenated analogs of tomoxetine that are potent and selective inhibitors of norepinephrine uptake in brain  
 AUTHOR(S): Gehlert, Donald R.; Schober, Douglas A.; Hemrick-Luecke, Susan K.; Krushinski, Joseph; Howbert, Jeffry; Robertson, David W.; Fuller, Ray W.; Wong, David T.  
 CORPORATE SOURCE: Central Nervous System Res., Lilly Research Lab., Indianapolis, IN, 46205, USA  
 SOURCE: Neurochemistry International (1995), 26(1), 47-52  
 CODEN: NEUIDS; ISSN: 0197-0186  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

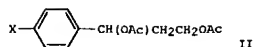
L9 ANSWER 83 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Binding to the dopamine transporter and inhibiting dopamine reuptake are considered important factors in regulating behavioral effects of cocaine. One prominent behavioral effect of cocaine and other dopamine uptake inhibitors is the stimulation of locomotor activity. To examine the relationship between action at the dopamine transporter and behavior, the displacement of [3H]WIN 35,428 (CFT naphthalene sulfate; 2- $\beta$ -carbomethoxy-3- $\beta$ -(4-fluorophenyl)tropane-1,5-naphthalene disulfonate) binding in rat caudate putamen by cocaine and other uptake inhibitors was compared with stimulation of mouse locomotor activity. There was a significant correlation among affinities for binding and potencies for stimulating activity for cocaine and structurally similar compds. For structurally dissimilar uptake inhibitors, however, there was no significant correlation among potencies for stimulation of activity and affinity for displacement of [3H]WIN 35,428 binding. These findings provide evidence that cocaine analogs may bind to the dopamine transporter in a manner that is fundamentally different from that for structurally dissimilar uptake inhibitors.

ACCESSION NUMBER: 1994:645160 CAPLUS  
 DOCUMENT NUMBER: 121:245160  
 TITLE: Differential relationships among dopamine transporter affinities and stimulant potencies of various uptake inhibitors  
 AUTHOR(S): Izenwasser, Sari; Terry, Philip; Heller, Brett; Witkin, Jeffrey M.; Katz, Jonathan L.  
 CORPORATE SOURCE: Psychobiology Section, National Institute on Drug Abuse, Intramural Research Program, National Institutes of Health, P.O. Box 5180, Baltimore, MD, 21224, USA  
 SOURCE: European Journal of Pharmacology (1994), 263(3), 277-83  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 85 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Using radioligand binding assays and post-mortem normal human brain tissue, the authors obtained equilibrium dissociation constants (K<sub>d</sub>s) for 17 antidepressants and two of their metabolites at histamine H<sub>1</sub>, muscarinic,  $\alpha$ 1-adrenergic,  $\alpha$ 2-adrenergic, dopamine D<sub>2</sub>, serotonin 5-HT<sub>1A</sub>, and serotonin 5-HT<sub>2</sub> receptors. Several newer antidepressants were compared with older drugs. In addition, the authors studied some antimuscarinic, antiparkinson, antihistamine, and neuroleptic compds. at some of these receptors. For the antidepressants, classical tricyclic antidepressants were the most potent drugs at five of the seven receptors (all but  $\alpha$ 2-adrenergic and 5-HT<sub>1A</sub> receptors). The chlorophenylpiperazine derivative etoperidone, nefazodone, trazodone) were the most potent antidepressants at  $\alpha$ 2-adrenergic and 5-HT<sub>1A</sub> receptors. Of ten antihistamines tested, none was more potent than doxepin at histamine H<sub>1</sub> receptors. At muscarinic receptors antidepressants and antihistamines had a range of potencies, which were mostly weaker than those for antimuscarinics. From the in vitro data, the authors expect adinazolam, bupropion, fluoxetine, sertraline, tomoxetine, and venlafaxine not to block any of these five receptors in vivo. An antidepressant's potency for blocking a specific receptor is predictive of certain side effects and drug-drug interactions. These studies can provide guidelines for the clinician in the choice of antidepressant.

ACCESSION NUMBER: 1994:449972 CAPLUS  
 DOCUMENT NUMBER: 121:49972  
 TITLE: Binding of antidepressants to human brain receptors: focus on newer generation compounds  
 AUTHOR(S): Cusack, Bernadette; Nelson, Albert; Richelson, Elliott  
 CORPORATE SOURCE: Dep. Res., Mayo Clin. Jacksonville, Jacksonville, FL, 32224, USA  
 SOURCE: Psychopharmacology (Berlin, Germany) (1994), 114(4), 559-65  
 CODEN: PSCHDL; ISSN: 0033-3158  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 84 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 GI



AB Optically active 1-aryl-1,3-propanediol (I: X=F or H) is prepared by enzymic resolution of 1-aryl-1,3-diacetoxypropane (II: X is same as above; Ac=acetyl) with (immobilized) lipase. I are useful intermediates for fluoxetine or tomoxetine. Preparation of R-1-phenyl-1,3-propanediol from racemic 1-phenyl-1,3-diacetoxypropane with lipase PS immobilized on  $\kappa$ -carrageenan was shown.

ACCESSION NUMBER: 1994:555916 CAPLUS  
 DOCUMENT NUMBER: 121:155916  
 TITLE: Enzymic resolution of 1-aryl-1,3-diacetoxypropane  
 INVENTOR(S): Miyazawa, Kazutoshi; Yoshida, Naoyuki; Sugura, Mitsuyo; Koizumi, Yasuyuki  
 PATENT ASSIGNEE(S): Chisso Corp, Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
| JP 06125789            | A2   | 19940510 | JP 1992-300685  | 19921014 |
| PRIORITY APPLN. INFO.: |      |          | JP 1992-300685  | 19921014 |

OTHER SOURCE(S): MARPAT 121:155916

L9 ANSWER 86 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Narcolepsy is currently treated with antidepressants to control REM-related symptoms such as cataplexy and with amphetamine-like stimulants for the management of sleepiness. Both stimulant and antidepressant drugs presynaptically enhance monoaminergic transmission but both classes of compds. lack pharmacol. specificity. In order to determine which monoamine is selectively involved in the therapeutic effect of these compds., the authors examined the effects of selective monoamine uptake inhibitors and release enhancers on cataplexy using a canine model of the human disorder. A total of 14 compds. acting on the adrenergic (desipramine, nioxetine, nortriptyline, tomoxetine, viloxazine), serotonergic (fenfluramine, fluoxetine, indalpine, paroxetine, zimelidine) and dopaminergic (amfonelic acid, amineptine, bupropion, GBR 12909) systems were tested. Some addnl. compds. interesting clin. but with less pharmacol. selectivity, i.e., cocaine, dextroamphetamine, methylphenidate, nomifensine and pemoline, were also included in the study. All compds. affecting noradrenergic transmission completely suppressed canine cataplexy at low doses in all dogs tested, whereas compds. which predominantly modified serotonergic and dopaminergic transmission were either inactive or partially active at high doses. The authors' results demonstrate the preferential involvement of adrenergic systems in the control of cataplexy and, presumably, REM sleep atonia. The authors' findings also demonstrate that canine narcolepsy is a useful tool in assessing the pharmacol. specificity of antidepressant drugs.

ACCESSION NUMBER: 1994:400675 CAPLUS  
 DOCUMENT NUMBER: 121:675  
 TITLE: Canine cataplexy is preferentially controlled by adrenergic mechanisms: evidence using monoamine selective uptake inhibitors and release enhancers  
 AUTHOR(S): Mignot, Emmanuel; Renaud, Alain; Nishino, Seiji; Arrigoni, Janis; Guilleminault, Christian; Dement, William C.  
 CORPORATE SOURCE: Sch. Med., Stanford Univ., Palo Alto, CA, 94304, USA  
 SOURCE: Psychopharmacology (Berlin, Germany) (1993), 113(1), 76-82  
 CODEN: PSCHDL; ISSN: 0033-3158  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 87 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Eight White Carneau pigeons were trained to discriminate 1.0 or 1.7 mg/kg of cocaine from saline. A fixed number of consecutive key peck responses on one key after the administration of cocaine resulted in 4-s access to mixed grain. The same number of consecutive responses on the other key after saline also produced food. Different doses of cocaine and other drugs were tested to determine their ability to substitute (80% or more responding on the cocaine-appropriate key). The test drugs were selected to determine the selectivity of the cocaine discrimination in pigeons as well the role of different monoamines in mediating this behavioral effect. The drugs included other psychomotor stimulants, antidepressants, clonidine, yohimbine, other dopamine ((1-2-[bis(4-(fluoro-phenyl)-methoxy)ethyl]4-3-phenylpropyl)piperazine, GBR 12909) and serotonin (5-HT, sertraline) reuptake blockers, a D1 (SKF 75670), D2 (quinpirole), and 5-HT1A (8-hydroxy-2-(di-n-propylamino)tetrallin, 8-PH-DPAT) agonist as well as the 5-HT3 antagonists, MDL 72222, LY 278584 and ondansetron. In addition, prazosin, an  $\alpha_1$  adrenergic antagonist, SCH 23390, a D1 antagonist; raclopride, a D2 antagonist and 1-(2-methoxyphenyl)-4-[4-(2-phthalimido)butyl]piperazine (NAN-190), a putative 5-HT1A antagonist, were given in combination with cocaine to determine their ability to block the discriminative stimulus (DS) effects of cocaine, i.e., reduce drug-appropriate responding to 20% or less. The psychomotor stimulants, d-amphetamine and d-methamphetamine, completely substituted for cocaine and were similar in potency to each other and cocaine. The antidepressants 1-deprenyl, imipramine, tomoxetine and bupropion also occasioned cocaine-appropriate responding. However, only partial substitution was seen with fluoxetine, clonidine, GBR 12909, quinpirole, SKF 75670 and 8-OH-DPAT. Responding occurred primarily on the saline-appropriate key after the administration of yohimbine, sertraline and the 5-HT3 antagonists. Prazosin, raclopride, SCH 23390 and NAN-190 blocked the DS effects of cocaine. Taken as a whole, these results indicate that the DS effects of cocaine are mediated not only by dopaminergic systems in the pigeon, as has been demonstrated in other species, but also at least in part by noradrenergic systems. Serotonin systems, in contrast, do not appear involved, although the results with fluoxetine, 8-OH-DPAT and NAN-190 warrant further investigation.

ACCESSION NUMBER: 1994:95445 CAPLUS  
 DOCUMENT NUMBER: 120:95445  
 TITLE: The discriminative stimulus effects of cocaine in pigeons  
 AUTHOR(S): Johanson, Chris Ellyn; Barrett, James E.  
 CORPORATE SOURCE: Dep. Psychiatry, Uniformed Serv. Univ. Health Sci., Bethesda, MD, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1993), 267(1), 1-8  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 89 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB The effects of norepinephrine (NE) reuptake inhibition on NE release and contractile responses in lower urinary tract tissues were evaluated using tomoxetine, a selective NE reuptake inhibitor, and imipramine, a nonselective reuptake inhibitor. Although both compounds significantly increased K<sup>+</sup>-evoked release of NE from urethral fragments obtained from rabbits, tomoxetine was at least 10X more potent than imipramine. Tomoxetine significantly enhanced the effects of NE to contract rabbit urethral fragments and to relax carbachol contracted rabbit bladder smooth muscle. Imipramine suppressed the effects of NE on urethral tissue and was less potent than tomoxetine in enhancing bladder responses to NE. These presynaptic and postsynaptic effects of NE reuptake inhibition in lower urinary tract tissues may contribute to the efficacy of imipramine in treating incontinence and represent a new clin. utility for selective and more potent reuptake inhibitors, such as tomoxetine.

ACCESSION NUMBER: 1993:487042 CAPLUS  
 DOCUMENT NUMBER: 119:87042  
 TITLE: Alterations in potassium-evoked release of 3H-norepinephrine and contractile responses in urethral and bladder tissues induced by reuptake inhibition  
 AUTHOR(S): Foreman, M. M.; McNulty, A. M.  
 CORPORATE SOURCE: Lilly Corp. Cent., Lilly Res. Lab., Indianapolis, IN, 46285, USA  
 SOURCE: Life Sciences (1993), 53(3), 193-200  
 CODEN: LIFSAK; ISSN: 0024-3205  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 88 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB The distribution of binding sites for the potent inhibitor of norepinephrine (NE) reuptake, [3H]tomoxetine, was examined in rat brain using quant. autoradiog. Scatchard anal. of [3H]tomoxetine-binding to slide-mounted sections of rat forebrain indicated that the ligand bound to 2 sites, a high-affinity site with a K<sub>d</sub> of 0.29 nM and a lower-affinity site with a K<sub>d</sub> of 16 nM. Pharmacol. characterization of this high-affinity site was consistent with labeling a NE-uptake site in brain. Autoradiog. localization of the binding sites for [3H]tomoxetine was performed at a ligand concentration of 1 nM representing the distribution of high-affinity sites. The radioligand bound with a distribution of binding sites that was consistent with the known distribution of NE-containing neurons. The highest levels of binding were seen in regions, such as the locus ceruleus, bed nucleus of the stria terminalis, anterior ventral nucleus of the thalamus and the paraventricular nucleus of the hypothalamus. Low levels were seen in regions such as the caudate-putamen, ventral tegmental area and zona reticulata of the substantia nigra, where NE-containing neurons have been reported to be low. Binding to all these sites was inhibited by 1  $\mu$ M desipramine which produced autoradiograms with a uniform nonspecific binding. Apparently, low concns. of [3H]tomoxetine can be used to localize and characterize NE-binding sites.

ACCESSION NUMBER: 1993:618089 CAPLUS  
 DOCUMENT NUMBER: 119:218089  
 TITLE: Localization of rat brain binding sites for [3H]tomoxetine, an enantiomerically pure ligand for norepinephrine reuptake sites  
 AUTHOR(S): Gehlert, Donald R.; Gackenhimer, Susan L.; Robertson, David W.  
 CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA  
 SOURCE: Neuroscience Letters (1993), 157(2), 203-6  
 CODEN: NELED5; ISSN: 0304-3940  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 90 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB We determined the uptake blockade produced by eight new antidepressant drugs (etoperidone, femoxetine, lofepramine, nefazodone, paroxetine, sertraline, tomoxetine, and venlafaxine), two metabolites of newer antidepressants, and carbamazepine. Inhibitor constants (K<sub>i</sub>s) for uptake blockade were obtained from competitive uptake studies with [3H]norepinephrine, [3H]5-hydroxytryptamine, and [3H]dopamine in rat brain synaptosomes prepared from hippocampus, frontal cortex, and striatum, resp. Among the newer compounds, tomoxetine (K<sub>i</sub> = 0.7 nM) and lofepramine (K<sub>i</sub> = 1.9 nM) were potent and selective [3H]norepinephrine uptake blockers; paroxetine (K<sub>i</sub> = 0.73 nM), sertraline (K<sub>i</sub> = 3.4 nM), and femoxetine (K<sub>i</sub> = 22 nM) potently and selectively inhibited [3H]5-hydroxytryptamine uptake. Although none of the drugs was potent for [3H]dopamine uptake blockade, sertraline was the most potent (K<sub>i</sub> = 260 nM). These data are useful in predicting adverse effects and drug-drug interactions of antidepressants.

ACCESSION NUMBER: 1993:183305 CAPLUS  
 DOCUMENT NUMBER: 118:183305  
 TITLE: Blockade by newly-developed antidepressants of biogenic amine uptake into rat brain synaptosomes  
 AUTHOR(S): Bolden-Watson, C.; Richelson, E.  
 CORPORATE SOURCE: Mayo Clin., Jacksonville, FL, 32224, USA  
 SOURCE: Life Sciences (1993), 52(12), 1023-9  
 CODEN: LIFSAK; ISSN: 0024-3205  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 91 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB A novel route for the synthesis of benzothioopyran and benzothiazepin ring systems along with the synthesis of optically pure, clin. effective drugs tomoxetine, fluoxetine and thiazesim is demonstrated.

ACCESSION NUMBER: 1993:101919 CAPLUS  
 DOCUMENT NUMBER: 118:101919  
 TITLE: A novel chemoenzymic enantioselective synthesis of some clinically effective CNS drugs and related compounds

AUTHOR(S): Kumar, Ashok; Ner, D. H.; Dike, Suneel  
 CORPORATE SOURCE: Alchemie Res. Cent., Thane, 400 601, India  
 SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1992), 31B(12), 803-9  
 CODEN: IJSBDB; ISSN: 0376-4699

DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 118:101919

L9 ANSWER 92 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Alcs. are acylated in the presence of a vinyl ester or carboxylic acid ester and Pseudomonas lipase immobilized on a polystyrene resin. The chiral products can be used in synthesis of protease inhibitors, non-steroidal anti-inflammatory drugs, beta-blockers, and other drugs. Geraniol was incubated with the lipase immobilized on Amberlite XAD-2 and vinyl acetate. A quant. yield of geraniol acetate was obtained in 1 h. When the enzyme was not immobilized, the same yield required 501 more time. The stability of the enzyme was also increased by immobilization.

ACCESSION NUMBER: 1992:632211 CAPLUS  
 DOCUMENT NUMBER: 117:232211  
 TITLE: Acylation of alcohols with immobilized Pseudomonas lipase

INVENTOR(S): Schudok, Manfred; Fuelling, Gerd; Kretzschmar, Gerhard  
 PATENT ASSIGNEE(S): Hoechst A.-G., Germany  
 SOURCE: Eur. Pat. Appl., 15 pp.  
 CODEN: EPXKDW

DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.                                | KIND | DATE     | APPLICATION NO. | DATE        |
|---|------|----------|-----------------|-------------|
| EP 492497                                 | A2   | 19920701 | EP 1991-121933  | 19911220    |
| EP 492497                                 | A3   | 19931020 |                 |             |
| EP 492497                                 | B1   | 19960828 |                 |             |
| R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL |      |          |                 |             |
| CA 2058185                                | AA   | 19920625 | CA 1991-2058185 | 19911220    |
| AT 141950                                 | E    | 19960915 | AT 1991-121933  | 19911220    |
| JP 04287689                               | A2   | 19921013 | JP 1991-340796  | 19911224    |
| JP 3117157                                | B2   | 20001211 |                 |             |
| US 5387514                                | A    | 19950207 | US 1993-173938  | 19931228    |
| PRIORITY APPLN. INFO.:                    |      |          | DE 1990-4041777 | A 19901224  |
|   |      |          | US 1991-806310  | B1 19911213 |

OTHER SOURCE(S): MARPAT 117:232211

L9 ANSWER 93 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Tomoxetine is useful for treatment of lower urinary tract disorders, e.g. urinary incontinence, detrusor instability, and interstitial cystitis. The preferred dosage is 0.5-20 mg/kg orally, rectally, topically, or parenterally.

ACCESSION NUMBER: 1992:563878 CAPLUS  
 DOCUMENT NUMBER: 117:163878  
 TITLE: tomoxetine for treatment of lower urinary tract disorders

INVENTOR(S): Foreman, Mark Mortensen  
 PATENT ASSIGNEE(S): Eli Lilly and Co., USA  
 SOURCE: Eur. Pat. Appl., 8 pp.  
 CODEN: EPXKDW

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE       |
|---|------|----------|-----------------|------------|
| EP 501705   | A1   | 19920902 | EP 1992-301494  | 19920224   |
| EP 501705   | B1   | 19960515 |                 |            |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE |      |          |                 |            |
| CA 2061665  | AA   | 19920826 | CA 1992-2061665 | 19920221   |
| CA 2061665  | C    | 20020416 |                 |            |
| AU 9211170  | A1   | 19920827 | AU 1992-111170  | 19920221   |
| AU 642582   | B2   | 19931021 |                 |            |
| ZA 9201292  | A    | 19930823 | ZA 1992-1292    | 19920221   |
| JP 05070343   | A2   | 19930323 | JP 1992-36029   | 19920224   |
| JP 3222524  | B2   | 20011029 |                 |            |
| HU 62192  | A2   | 19930428 | HU 1992-602     | 19920224   |
| HU 215122   | B    | 19980928 |                 |            |
| AT 137963   | E    | 19960615 | AT 1992-301494  | 19920224   |
| US 5441985  | A    | 19950815 | US 1993-61335   | 19930513   |
| PRIORITY APPLN. INFO.:  |      |          | US 1991-660767  | A 19910225 |

L9 ANSWER 94 OF 106 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB The tricyclic antidepressant imipramine was established as a discriminative stimulus in pigeons at two doses (3.0 or 5.6 mg/kg). Because imipramine has multiple effects on different neurotransmitter systems, a range of compds. from several pharmacol. classes were tested for substitution. The tricyclic antidepressants desipramine, amitriptyline and doxepine, all of which block serotonin (5-HT) and norepinephrine (NE) reuptake, resulted in imipramine-key responding. The psychomotor stimulants cocaine and d-amphetamine also occasioned responding on the imipramine key, as did the NE reuptake inhibitor tomoxetine; nomifensine, which blocks the reuptake of both NE and dopamine (DA), also resulted in responding on the key correlated with imipramine injections. Bupropion, a DA reuptake inhibitor, resulted in drug key responding but substitution did not occur with another DA uptake inhibitor GBR 12909. The alpha-2 agonist clonidine, the 5-HT2 antagonist ritanserin or the 5-HT reuptake inhibitor fluoxetine also did not occasion drug-key responding. Drug-appropriate responding occurred in pigeons trained at the lower dose of imipramine with the 5-HT1A compds. 8-hydroxy-2-(di-n-propylamino)tetrailin hydrobromide and gepirone; partial substitution occurred in pigeons trained with the higher dose of imipramine. Substitution for the imipramine stimulus by gepirone, an antidepressant with actions mediated by the 5-HT1A receptor, as well as with 8-hydroxy-2-(di-n-propylamino)tetrailin hydrobromide, suggests that imipramine may have effects at this receptor site and confirms reports that compds. active at this receptor may have antidepressant activity. This appears to be the first report of the successful long-term establishment of imipramine as a discriminative stimulus without the development of toxicity. These results indicate that the discriminative stimulus effects of imipramine are complex and involve at least NE reuptake and a specific 5-HT receptor subtype (1A). Generalization to the imipramine stimulus by cocaine and d-amphetamine also suggests that further analyses of these drugs as discriminative stimuli, with particular attention to the possible role of the 5-HT1A receptor and NE systems, may aid in clarifying their neurochem. and behavioral actions as abused drugs.

ACCESSION NUMBER: 1992:76250 CAPLUS  
 DOCUMENT NUMBER: 116:76250  
 TITLE: Imipramine as a discriminative stimulus

AUTHOR(S): Zhang, L.; Barrett, J. E.  
 CORPORATE SOURCE: Dep. Psychiatry, Uniformed Serv. Univ. Health Sci., Bethesda, MD, 20814-4799, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1991), 259(3), 1088-93  
 CODEN: JPETAB; ISSN: 0022-3565

DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 95 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Rhesus monkeys trained in a two-lever, food-reinforced paradigm to discriminate cocaine (0.2 or 0.4 mg/kg, i.m.) from saline, received injections of cocaine (0.025-0.40 mg/kg, i.v. or i.m.) or various direct and indirect acting agonists (i.v.). Administration of cocaine resulted in a dose-related increase in the percentage of responses that occurred on the drug-appropriate lever. The indirect dopamine agonists GBR 12909 (0.2-1.6 mg/kg), mazindol (0.025-0.4 mg/kg), nomifensine (0.025-0.2 mg/kg) and bupropion (0.1-1.6 mg/kg) each produced dose-related increase in cocaine-appropriate responding, with complete substitution for cocaine achieved at the highest doses of each drug. In contrast, the norepinephrine re-uptake blockers tomozetidine (0.8-6.4 mg/kg) and nisoxetine (0.4-1.6 mg/kg), the serotonin re-uptake blocker fluoxetine (1.6-12.8 mg/kg), the D1 agonist SKF 38393 (3.2-12.8 mg/kg) and the D2 agonist quinpirole (0.05-0.2 mg/kg) failed to engender cocaine-appropriate responding. Administration of the D1 antagonist SCH 23390 (0.05-0.2 mg/kg, i.m.) 20 min before cocaine resulted in a 4- to 8-fold parallel shift to the right in the cocaine dose-response function. Similarly, the D2 antagonist haloperidol (0.003-0.012 mg/kg, i.m.) produced at least 2-fold shift to the right in the cocaine dose-response function. The results indicate that blockade of dopamine re-uptake is sufficient to mimic the cocaine discriminative stimulus and suggest that stimulation of either D1 or D2 receptors is necessary but not sufficient for the expression of the discriminative stimulus effects of cocaine.

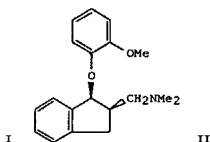
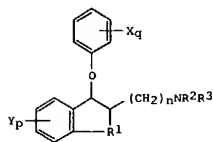
ACCESSION NUMBER: 1990:526451 CAPLUS  
 DOCUMENT NUMBER: 113:126451  
 TITLE: Pharmacological characterization of the discriminative stimulus effects of cocaine in rhesus monkeys  
 AUTHOR(S): Kleven, Mark S.; Anthony, Elizabeth W.; Woolverton, William L.  
 CORPORATE SOURCE: Dep. Pharmacol. Physiol. Sci., Univ. Chicago, Chicago, IL, 60637, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1990), 254(1), 312-17  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 96 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Optically active alcs. R1R2CHOR [I; R1 = (halogen substituted) C1-18 alkyl, C6-10 cycloalkyl; R2 = epoxy-C1-5 alkyl; (substituted) C1-10 alkyl, C2-10 alkenyl or alkynyl, C3-8 cycloalkenyl] are produced from the racemic alc. and a vinyl ester CH2:CHR3OC(=O)R4 [II; R3 = H, Me; R4 = H, (halogen-substituted) C1-8 alkyl, Ph, C1-3 alkoxy-C1-4 alkyl; R3,R4 together = alkenylene] with a lipase from swine liver or pancreas, or from microorganisms such as Candida, Mucor, etc. The optically active alcs. may be used to prepare nonsteroidal anti-inflammatory drugs,  $\beta$ -blockers, bronchospasmolytics, antimycotics, pyrethroids, prostaglandins, carbohydrates, etc. Vinyl acetate or vinyl chloroacetate and 31 different alcs. were incubated with Lipase P or FP to prepare optically active alcs. in yields varying from 28-98% and enantiomeric excess of 23-98%.

ACCESSION NUMBER: 1990:137568 CAPLUS  
 DOCUMENT NUMBER: 112:137568  
 TITLE: Process for the enzymatic resolution of racemic alcohols with/in vinyl esters by transesterification  
 INVENTOR(S): Keller, Reinhold; Holla, Wolfgang; Fuelling, Gerd  
 PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.  
 SOURCE: Eur. Pat. Appl., 12 pp. CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.                        | KIND | DATE     | APPLICATION NO.   | DATE       |
|-----------------------------------|------|----------|-------------------|------------|
| EP 321918                         | A2   | 19890628 | EP 1988-121274    | 19881220   |
| EP 321918                         | A3   | 19901003 |                   |            |
| EP 321918                         | B1   | 19940323 |                   |            |
| EP 321918                         | B2   | 19990414 |                   |            |
| R: BE, CH, DE, FR, GB, IT, LI, NL |      |          |                   |            |
| DE 3743824                        | A1   | 19890706 | DE 1987-3743824   | 19871223   |
| DE 3743824                        | C2   | 19970306 |                   |            |
| US 4963492                        | A    | 19901016 | US 1988-287371    | 19881221   |
| JP 01202296                       | A2   | 19890815 | JP 1988-322246    | 19881222   |
| JP 07002118                       | B4   | 19950118 |                   |            |
| PRIORITY APPLN. INFO.:            |      |          | DE 1987-3743824   | A 19871223 |
| OTHER SOURCE(S):                  |      |          | MARPAT 112:137568 |            |

L9 ANSWER 97 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB Title compds. I [R1 = C1-3 alkylene; n, p, q = 0-2; X, Y = C1-6 alkyl or alkoxy, OH, CF3, halo; or (X)2, (Y)2 = OCH2O; R2, R3 = H, C1-6 alkyl, aralkyl; or NR2R3 = pyrrolidino, morpholino, piperidino, piperazino, 4-methylpiperazino] were prepared as antidepressants (no data). In addition, administering uptake inhibitors of both norepinephrine and serotonin produced synergistic down-regulation of  $\beta$ -adrenergic receptors in rats. Reduction of 2,3-dihydro-2-(N,N-dimethylaminomethyl)-1H-inden-1-one-HCl by L-Selectride in THF gave 48% of the cis alc., which was etherified with 2-FC6H4OMe using NaH in Me2SO to give cis-dihydro(methoxyphenoxy)dimethylindanemethanamine II. In a sep. rat experiment combined treatment with desipramine (5 mg/kg, i.p.) and fluoxetine (10 mg/kg, i.p.) for 14 days down-regulated cortical  $\beta$ -adrenergic receptor number to 64% of control, vs. only 86% and 91% by the resp. drugs alone.

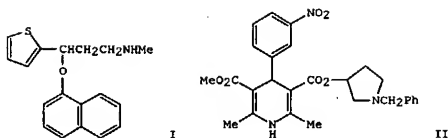
ACCESSION NUMBER: 1989:533804 CAPLUS  
 DOCUMENT NUMBER: 111:133804  
 TITLE: Preparation and formulation of (aryloxy)indanamines and related compounds useful as antidepressants and as inhibitors of synaptic norepinephrine and serotonin uptake  
 INVENTOR(S): Freedman, Jules; Dudley, Mark W.  
 PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Inc., USA  
 SOURCE: Eur. Pat. Appl., 15 pp. CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| EP 303961   | A2   | 19890222 | EP 1988-112996  | 19880810 |
| EP 303961   | A3   | 19900517 |                 |          |
| EP 303961   | B1   | 19940413 |                 |          |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                 |          |
| ZA 8805824  | A    | 19890426 | ZA 1988-5824    | 19880808 |
| CA 1327795  | A1   | 19940315 | CA 1988-574102  | 19880808 |

L9 ANSWER 97 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE        |
|------------------------|------|----------|-----------------|-------------|
| AU 8820579             | A1   | 19890216 | AU 1988-20579   | 19880809    |
| AU 606444              | B2   | 19910207 |                 |             |
| AT 104269              | E    | 19940415 | AT 1988-112996  | 19880810    |
| ES 2054747             | T3   | 19940816 | ES 1988-112996  | 19880810    |
| FI 8803739             | A    | 19890215 | FI 1988-3739    | 19880811    |
| FI 91852               | B    | 19940513 |                 |             |
| FI 91852               | C    | 19940825 |                 |             |
| JP 01066151            | A2   | 19890313 | JP 1988-199045  | 19880811    |
| JP 2650045             | B2   | 19970903 |                 |             |
| IL 87412               | A1   | 19950526 | IL 1988-87412   | 19880811    |
| DK 8804546             | A    | 19890215 | DK 1988-4546    | 19880812    |
| NO 8803595             | A    | 19890215 | NO 1988-3595    | 19880812    |
| NO 167913              | B    | 19910916 |                 |             |
| NO 167913              | C    | 19911227 |                 |             |
| HU 51593               | A2   | 19900528 | HU 1988-4347    | 19880812    |
| HU 204504              | B    | 19920128 |                 |             |
| CN 1033043             | A    | 19890524 | CN 1988-106476  | 19880813    |
| CN 1021323             | B    | 19930623 |                 |             |
| KR 126137              | B1   | 19971226 | KR 1988-10350   | 19880813    |
| US 5149714             | A    | 19920922 | US 1990-569259  | 19900815    |
| US 5561152             | A    | 19961001 | US 1994-350236  | 19941206    |
| US 5880120             | A    | 19990309 | US 1997-937224  | 19970911    |
| US 6136803             | A    | 20001024 | US 1998-209200  | 19981210    |
| PRIORITY APPLN. INFO.: |      |          | US 1987-85665   | A 19870814  |
|                        |      |          | EP 1988-112996  | A 19880810  |
|                        |      |          | US 1988-287517  | B3 19881219 |
|                        |      |          | US 1989-296474  | B1 19890112 |
|                        |      |          | US 1989-401518  | B2 19890829 |
|                        |      |          | US 1989-434665  | B1 19891113 |
|                        |      |          | US 1990-569259  | A1 19900815 |
|                        |      |          | US 1991-762050  | B1 19910918 |
|                        |      |          | US 1992-820475  | B1 19920114 |
|                        |      |          | US 1992-855125  | B1 19920318 |
|                        |      |          | US 1992-979357  | B1 19921120 |
|                        |      |          | US 1993-46104   | B1 19930408 |
|                        |      |          | US 1993-133829  | B1 19931007 |
|                        |      |          | US 1993-170437  | B1 19931220 |
|                        |      |          | US 1994-278697  | B1 19940721 |
|                        |      |          | US 1994-294774  | B1 19940823 |
|                        |      |          | US 1995-440511  | B1 19950512 |
|                        |      |          | US 1996-733901  | B1 19961018 |

OTHER SOURCE(S): MARPAT 111:133804



AB HPLC methods were developed to sep. some CNS drugs, both indirectly after diastereomer formation, and directly using chiral stationary phases.

Some examples are: resolution of fluoxetine as mandelic acid derivative on a H2 column; resolution and determination of I as Mosher's acid derivative on a NH2 column or the acetylate I derivative on a Cyclobond I column; chromatog. of tomoxetine spiked with its (+)-isomer on a Cyclobond I column after acetylation; and chiral separation of the Ca channel blocker II on an  $\alpha$ -acid glycoprotein column.

ACCESSION NUMBER: 1988:535063 CAPLUS  
DOCUMENT NUMBER: 109:135063  
TITLE: Practical considerations for chiral separations of pharmaceutical compounds  
AUTHOR(S): Bopp, Ronald J.; Kennedy, Joseph H.  
CORPORATE SOURCE: Lilly Corp. Cent., Eli Lilly Co., Indianapolis, IN, 46285, USA  
SOURCE: LC-GC (1988), 6(6), 514, 516, 518, 520, 522  
CODEN: LCGCE7; ISSN: 0888-9090  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L9 ANSWER 99 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB A polemic. The comparison between R-(-)-tomoxetine (R-(-)-I) and R-(-)-noradrenaline (R-(-)-II) as presented by Wong et al (ibid. 1982, 222, 61-65) is not valid due to the change in priorities in numbering the groups attached to the chiral centers of these 2 mols. Thus the biol. relevant R-(-)-isomer of II has the same configuration as the less active S-(+)-isomer of I and S-(-)-isomer of nisoxetine.

ACCESSION NUMBER: 1988:16321 CAPLUS  
DOCUMENT NUMBER: 108:16321  
TITLE: Tomoxetine and the stereoselectivity of drug action  
AUTHOR(S): Oberlander, Robert; Nichols, David E.; Ramachandran, P. V.; Srebnik, Morris; Brown, H. C.; Wetherill, R.  
B.  
CORPORATE SOURCE: Sch. Pharm. Pharmacol Sci., Purdue Univ., West Lafayette, IN, 47907, USA  
SOURCE: Journal of Pharmacy and Pharmacology (1987), 39(12), 1055-6  
CODEN: JPPMAB; ISSN: 0022-3573  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L9 ANSWER 100 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
AB (+)-2-MeC6H4OCH(Ph)CH2CH2NHMe [(+)-I], the racemate of the antidepressant tomoxetine ((-)-I), is prepared by reacting (+)-I with RM (R = alkyl, alkylamide; M = alkali metal) in MeOCH2CH2OMe or THF under inert conditions. Thus, BuLi in hexane was added over 5 min to (+)-I in THF at 17-22° and the mixture stirred for .apprx.3.5 h to give 97% (+)-I. Resolution of (+)-I gave 49% (-)-I.L-(+)-mandelic acid, which was hydrolyzed by NaOH in Et2O and acidified to give 62.7% (-)-I.

ACCESSION NUMBER: 1986:626035 CAPLUS  
DOCUMENT NUMBER: 105:226035  
TITLE: Racemization of tomoxetine enantiomer  
INVENTOR(S): Misner, Jerry Wayne  
PATENT ASSIGNEE(S): Eli Lilly and Co., USA  
SOURCE: Eur. Pat. Appl., 22 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE       |
|------------------------|------|----------|-----------------|------------|
| EP 193405              | A1   | 19860903 | EP 1986-301417  | 19860227   |
| EP 193405              | B1   | 19890308 |                 |            |
| US 4777291             | A    | 19881011 | US 1985-706373  | 19850227   |
| CA 1269997             | A1   | 19900605 | CA 1986-502597  | 19860225   |
| JP 61210059            | A2   | 19860918 | JP 1986-42792   | 19860226   |
| HU 42055               | A2   | 19870629 | HU 1986-815     | 19860226   |
| HU 196586              | B    | 19881228 |                 |            |
| AT 41144               | E    | 19890315 | AT 1986-301417  | 19860227   |
| PRIORITY APPLN. INFO.: |      |          | US 1985-706373  | A 19850227 |
|                        |      |          | EP 1986-301417  | A 19860227 |

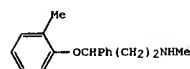


L9 ANSWER 101 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Antidepressants interacted competitively with putative adenosine transport sites and adenosine receptors of rat brain membranes in a study of the abilities of 12 antidepressants to compete with 3H-labeled nitrobenzylthioinosine [38048-32-7] binding to putative adenosine transport sites and with 3H-labeled cyclohexyladenosine (II) [36396-99-3] binding to adenosine receptors. Chronic treatment of rats with doxepin [1668-19-5] increased the number of adenosine receptors (as determined by II binding to receptor sites of the brain). Brain adenosine deaminase [9026-93-1] was not affected by 5 of the antidepressants (clogargine [17780-72-2], amitriptyline [50-48-6], zimelidine [56775-88-3], and doxepin).  
 ACCESSION NUMBER: 1986:527404 CAPLUS  
 DOCUMENT NUMBER: 105:127404  
 TITLE: Antidepressant competition for adenosine binding sites and chronic doxepin induced increases in adenosine receptors  
 AUTHOR(S): Lewis, J. L.; Geiger, J. D.  
 CORPORATE SOURCE: Fac. Med., Univ. Manitoba, Winnipeg, MB, R3E 0W3, Can.  
 SOURCE: Proceedings of the Western Pharmacology Society (1986), 29, 265-9  
 CODEN: FWPSAB; ISSN: 0083-8969  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

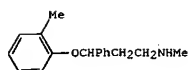
L9 ANSWER 102 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A pharmacokinetic profile of tomoxetine [83015-26-3], a selective norepinephrine uptake inhibitor, was developed in human volunteers following single and multiple oral administrations. Following the administration of a single 90-mg oral dose of tomoxetine to 4 normal volunteers, the plasma half-life was 4.3 h. Mean plasma clearance was 0.60 L/kg/h, and the mean volume of distribution was 3.7 L/kg. When 2 doses per day (20 mg and 40 mg) were administered for 7 days, the data appeared to have bimodal distribution. The mean plasma half-life determined following the last dose was 4.6 h in 5 subjects. The other 2 subjects, 1 at each dose level, demonstrated accumulation of tomoxetine occurring from the first to last dose where tomoxetine disappeared from plasma with a mean half-life of 19 h.  
 ACCESSION NUMBER: 1985:515611 CAPLUS  
 DOCUMENT NUMBER: 103:115611  
 TITLE: Single-dose and steady-state pharmacokinetics of tomoxetine in normal subjects  
 AUTHOR(S): Farid, Nagy A.; Bergstrom, Richard F.; Ziege, Edgar A.; Parli, C. John; Lemberger, Louis  
 CORPORATE SOURCE: Lilly Lab. Clin. Res., Eli Lilly Co., Indianapolis, IN, USA  
 SOURCE: Journal of Clinical Pharmacology (1985), 25(4), 296-301  
 CODEN: JCPCBR; ISSN: 0091-2700  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 103 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The effects of daily administration to rats of desipramine [50-47-5], talsupram [21489-20-3], tomoxetine [83015-26-3], maprotiline [10262-69-8], nomifensine maleate [32795-47-4] mianserin [24219-97-4] and citalopram [59729-33-8] (each 10 mg kg<sup>-1</sup> day<sup>-1</sup>) for 4 wk on [3H]dihydroalprenolol ([3H]DHA) binding in the cerebral cortex and on the noradrenaline [51-41-2]-sensitive adenylate cyclase [9012-42-4] in the limbic forebrain were determined. Of these compounds, only desipramine reduced [3H]DHA binding and attenuated the cAMP [60-92-4] response. Two selective noradrenaline uptake inhibitors, talsupram and tomoxetine each reduced the cAMP response but without affecting [3H]DHA binding. The other drugs lacked effect on both measures indicating (except for citalopram) that reduction in sensitivity of  $\beta$ -adrenoceptors and of the noradrenaline-sensitive cAMP response might not be a simple consequence of noradrenaline uptake inhibition. The lack of effect of citalopram on the sensitivity of the  $\beta$ -adrenoceptor system suggests that antidepressants with selective 5-HT [50-67-3] uptake inhibitory properties owe their antidepressant activity to other mechanisms.  
 ACCESSION NUMBER: 1985:160303 CAPLUS  
 DOCUMENT NUMBER: 102:160303  
 TITLE: Effects of some atypical antidepressants on  $\beta$ -adrenoceptor binding and adenylate cyclase activity in the rat forebrain  
 AUTHOR(S): Garcha, Gurbakhsh; Smokum, Roger W. J.; Stephenson, John D.; Weeramanthri, Tara B.  
 CORPORATE SOURCE: Dep. Pharmacol., Inst. Psychiatry, London, SE5 8AF, UK  
 SOURCE: European Journal of Pharmacology (1985), 108(1), 1-7  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L9 ANSWER 104 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB Tomoxetine (I) [83015-26-3] was administered in single oral doses up to 90 mg to healthy normal volunteers. In addition, normal human subjects received either 20 or 40 mg of tomoxetine twice a day (b.i.d.) for 1 wk to evaluate the safety and pharmacol. activity of the compound in humans. At these doses, no serious drug-related adverse effects were encountered. Activity of the compound at the lower dose (20 mg b.i.d.) was evaluated by examining changes in the pressor responses to infused norepinephrine and tyramine and by determining [3H]serotonin uptake in platelets harvested from subjects receiving the compound. Pressor sensitivity to norepinephrine was increased by 26% of control, and pressor sensitivity to tyramine was decreased by 51% of control during treatment. Changes in the pressor sensitivity to norepinephrine in individual subjects were correlated with drug levels. There were no statistically significant changes in platelet [3H]serotonin uptake. Apparently, tomoxetine selectively inhibits norepinephrine uptake in humans at doses which are clin. well tolerated and tomoxetine has potential clin. use as an antidepressant.  
 ACCESSION NUMBER: 1985:106154 CAPLUS  
 DOCUMENT NUMBER: 102:106154  
 TITLE: Clinical pharmacology of tomoxetine, a potential antidepressant  
 AUTHOR(S): Zerbe, Robert L.; Rowe, Howard; Enas, Gregory G.; Wong, David; Farid, Nagy; Lemberger, Louis  
 CORPORATE SOURCE: Lilly Lab. Clin. Res., Eli Lilly and Co., Indianapolis, IN, 46205, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1985), 232(1), 139-43  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

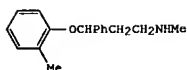


AB Tomoxetine (I) [83015-26-3], a potential antidepressant drug, antagonized the  $\alpha$ -methyl-m-tyrosine-induced depletion of hypothalamic epinephrine [51-43-4] and norepinephrine [51-41-2] in rats.

The findings suggest that tomoxetine, like several uptake-inhibiting antidepressant drugs, inhibits uptake into epinephrine neurons as well as into norepinephrine neurons in brain.

ACCESSION NUMBER: 1981:533530 CAPLUS  
DOCUMENT NUMBER: 99:133530  
TITLE: Antagonism by tomoxetine of the depletion of norepinephrine and epinephrine in rat brain by  $\alpha$ -methyl-m-tyrosine

AUTHOR(S): Fuller, Ray W.; Hemrick-Luecke, Susan K.  
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA  
SOURCE: Research Communications in Chemical Pathology and Pharmacology (1983), 41(1), 169-72  
CODEN: RCOCB8; ISSN: 0034-5164  
DOCUMENT TYPE: Journal  
LANGUAGE: English



AB The levorotatory form of amine I was prepared, and (-)-I·HCl (II) exhibited antidepressant activity (formulations are given). Thus, 2-MeC6H4OCHPhCH2CH2NHMe2 was converted to 2-MeC6H4OCHPhCH2CH2NHMeCO2Ph, the latter was deacylated to racemic I·HCl, and resolution with L(+)-mandelic acid gave II.

ACCESSION NUMBER: 1982:615718 CAPLUS  
DOCUMENT NUMBER: 97:215718  
TITLE: 3-Aryloxy-3-phenylpropylamines  
INVENTOR(S): Foster, Bennie Joe; Lavagnino, Edward Ralph  
PATENT ASSIGNEE(S): Eli Lilly and Co., USA  
SOURCE: Eur. Pat. Appl., 29 pp.  
CODEN: EPXKDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.                                | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| EP 52492                                  | A1   | 19820526 | EP 1981-305387  | 19811113 |
| EP 52492                                  | B1   | 19840229 |                 |          |
| R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE |      |          |                 |          |
| FI 8103589                                | A    | 19820515 | FI 1981-3589    | 19811112 |
| FI 77018                                  | B    | 19880930 |                 |          |
| FI 77018                                  | C    | 19890110 |                 |          |
| AU 8177427                                | A1   | 19820520 | AU 1981-77427   | 19811112 |
| AU 540707                                 | B2   | 19841129 |                 |          |
| ZA 8107863                                | A    | 19830629 | ZA 1981-7863    | 19811112 |
| RO 83309                                  | P    | 19840221 | RO 1981-105785  | 19811112 |
| CA 1181430                                | A1   | 19850122 | CA 1981-389954  | 19811112 |
| DK 8105027                                | A    | 19820515 | DK 1981-5027    | 19811113 |
| DK 161887                                 | B    | 19910826 |                 |          |
| DK 161887                                 | C    | 19920316 |                 |          |
| GB 2087883                                | A    | 19820603 | GB 1981-34282   | 19811113 |
| JP 57114555                               | A2   | 19820716 | JP 1981-182953  | 19811113 |
| JP 03069885                               | B4   | 19911105 |                 |          |
| ES 507142                                 | A1   | 19820816 | ES 1981-507142  | 19811113 |
| DD 201139                                 | C    | 19830706 | DD 1981-234837  | 19811113 |
| SU 1068034                                | A3   | 19840115 | SU 1981-3355735 | 19811113 |
| AT 6422                                   | E    | 19840315 | AT 1981-305387  | 19811113 |
| HU 30622                                  | O    | 19840328 | HU 1981-3411    | 19811113 |
| HU 185475                                 | B    | 19850228 |                 |          |
| CS 227019                                 | P    | 19840416 | CS 1981-8359    | 19811113 |
| HU 32779                                  | O    | 19840928 | HU 1983-4481    | 19811113 |
| IL 64288                                  | A1   | 19850430 | IL 1981-64288   | 19811115 |
| JP 03007250                               | A2   | 19910114 | JP 1990-147166  | 19900605 |
| JP 04006698                               | B4   | 19920206 |                 |          |
| JP 03007251                               | A2   | 19910114 | JP 1990-147167  | 19900605 |

=>  
Connection closed by remote host

---Logging off of STN---

END

Unable to generate the STN prompt.  
Exiting the script...  
<-----User Break----->

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1204bxd

PASSWORD:

\* \* \* \* \* RECONNECTED TO STN INTERNATIONAL \* \* \* \* \*  
SESSION RESUMED IN FILE 'CAPLUS' AT 18:10:12 ON 06 DEC 2004  
FILE 'CAPLUS' ENTERED AT 18:10:12 ON 06 DEC 2004  
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)  
COST IN U.S. DOLLARS

|                     | SINCE FILE | TOTAL   |
|---------------------|------------|---------|
|                     | ENTRY      | SESSION |
| FULL ESTIMATED COST | 304.74     | 312.41  |

|  | SINCE FILE | TOTAL   |
|--|------------|---------|
|  | ENTRY      | SESSION |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) |            |         |
| CA SUBSCRIBER PRICE                        | -76.30     | -76.30  |

=> d his

(FILE 'HOME' ENTERED AT 17:50:50 ON 06 DEC 2004)

FILE 'REGISTRY' ENTERED AT 17:50:54 ON 06 DEC 2004

L1 1 S ATOMOXETINE/CN

FILE 'CAPLUS' ENTERED AT 17:52:29 ON 06 DEC 2004

L2 50 S ATOMOX?  
L3 50 S ATOMOXETINE  
L4 107 S 83015-26-3/RN  
L5 3 S 83015-26-3D/RN  
L6 109 S L4 OR L5  
L7 143300 S SEX?  
L8 3 S L6 AND L7  
L9 106 S L6 NOT L8

=> s norephinephrine

L10 131 NOREPHINEPHRINE

=> s l10 and l7

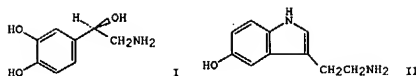
L11 3 L10 AND L7

=> d l11 1-3 abs ibib



L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB In the present experiment, 6-OHDA was infused directly into the olfactory bulb (OB) to produce a localized neurotoxic lesion. Habituation/dishabituation behavioral tests were then conducted to measure recognition responses to chemical cues (urine as a stimulus) and to social stimuli (ovariectomized rat as a stimulus). Infusion of 6-OHDA resulted in a near complete depletion of OB-norepinephrine (NE), whereas it had little effect (15% reduction) on OB dopamine (DA) contents. Nor were any significant effects on hypothalamic, hippocampal, olfactory tubercle, and corpus striatal NE and DA contents observed. Behaviorally, dishabituation responses to chemical cues were greatly impaired, however there was relatively little effect on social behavior dishabituation responses. These results demonstrate that 6-OHDA can be used to produce a near complete but localized depletion of OB-NE. This treatment impairs dishabituation responses to chemical cues but not social stimuli indicating that OB-NE appears necessary for processing of chemical cue, but not social memory recognition process.  
 ACCESSION NUMBER: 1993:596325 CAPLUS  
 DOCUMENT NUMBER: 119:196325  
 TITLE: Depletion of olfactory bulb norepinephrine by 6-OHDA disrupts chemical cue but not social recognition responses in male rats  
 AUTHOR(S): Guan, Xiaobin; Blank, James; Dluzen, Dean  
 CORPORATE SOURCE: Department of Anatomy, Northeastern Ohio Universities,  
 College of Medicine, Rootstown, OH, 44272, USA  
 SOURCE: Brain Research (1993), 622(1-2), 51-7  
 CODEN: BRBEP; ISSN: 0006-8993  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB In brain synaptosomes from inbred mice (C57 strain) both noradrenaline (I) [51-41-2] and serotonin (II) [50-67-9] uptake was characterized by a high level of homogeneity with no variance with respect to hypothetical fluctuations in the methods used to measure such uptake, suggesting that interindividual differences found in uptake are not due to poor reliability in tech. procedures. In rats I uptake was affected by interindividual differences in synaptosomal preps. as well as sex of the animal. Synaptosomes from male rats incorporated less I than did those from females.  
 ACCESSION NUMBER: 1979:551743 CAPLUS  
 DOCUMENT NUMBER: 91:151743  
 TITLE: Multivariate approaches applied to studies of norepinephrine and serotonin in uptake  
 AUTHOR(S): Sacchetti, E.; Allaria, E.; Conte, G.; De Rosa, A.; Griffi, P. G.; Taroni, P. L.; Resele, L.; Smeraldi, E.  
 CORPORATE SOURCE: Med. Sch., Milan Univ., Milan, Italy  
 SOURCE: Developments in Psychiatry (1979), Volume Date 1978, 2(Biol. Psychiatry Today, Vol. A), 137-41  
 CODEN: DPSYDX; ISSN: 0166-2481  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Castration of rats immediately after birth, which induces a permanent feminization of reproductive function, resulted in a marked reduction in the weight and total organ content of norepinephrine in the vasa deferentia as measured before and after sexual maturation. The norepinephrine fall was approx. 3-fold greater than after castration of adult animals. Androgenization of female rats by a single injection of testosterone propionate on the 5th day post partum did not affect uterine weight, but significantly lowered total organ content of norepinephrine when measured before and after sexual maturation. Thus, the vasa deferentia and uterus contain a population of adrenergic nerves, probably identical with or part of the system of short adrenergic neurons that constitute a sep. target system for those humoral factors which determine the pattern of development of the reproductive tract by influencing the early differentiation of the hypothalamus.  
 ACCESSION NUMBER: 1974:518002 CAPLUS  
 DOCUMENT NUMBER: 81:118002  
 TITLE: Consequence of neonatal androgenization and castration for future levels of norepinephrine transmitter in uterus and vas deferens of the rat  
 AUTHOR(S): Broberg, A.; Nybell, G.; Owan, Ch.; Rosengren, E.; Sjöberg, N. O.  
 CORPORATE SOURCE: Dep. Histol., Univ. Lund, Lund, Swed.  
 SOURCE: Neuroendocrinology (1974), 15(5), 308-12  
 CODEN: NUNDAJ; ISSN: 0028-3835  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

```
=> s "norepinephrine transport inhibitor"
      131 "NOREPINEPHRINE"
      633051 "TRANSPORT"
      4900 "TRANSPORTS"
      634978 "TRANSPORT"
            ("TRANSPORT" OR "TRANSPORTS")
      458835 "INHIBITOR"
      476211 "INHIBITORS"
      736009 "INHIBITOR"
            ("INHIBITOR" OR "INHIBITORS")
L12      0 "NOREPINEPHRINE TRANSPORT INHIBITOR"
          ("NOREPINEPHRINE" (W) "TRANSPORT" (W) "INHIBITOR")
```

```
=> d his
```

```
(FILE 'HOME' ENTERED AT 17:50:50 ON 06 DEC 2004)
```

```
FILE 'REGISTRY' ENTERED AT 17:50:54 ON 06 DEC 2004
```

```
L1      1 S ATOMOXETINE/CN
```

```
FILE 'CAPLUS' ENTERED AT 17:52:29 ON 06 DEC 2004
```

```
L2      50 S ATOMOX?
L3      50 S ATOMOXETINE
L4      107 S 83015-26-3/RN
L5      3 S 83015-26-3D/RN
L6      109 S L4 OR L5
L7      143300 S SEX?
L8      3 S L6 AND L7
L9      106 S L6 NOT L8
L10     131 S NOREPINEPHRINE
L11     3 S L10 AND L7
L12     0 S "NOREPINEPHRINE TRANSPORT INHIBITOR"
```

```
=> s noradrenergic
      11336 NORADRENERGIC
      1 NORADRENERGICS
L13     11336 NORADRENERGIC
          (NORADRENERGIC OR NORADRENERGICS)
```

```
=> s l13 and l7
L14     287 L13 AND L7
```

```
=> s l14 and l10
L15     1 L14 AND L10
```

```
=> d l15 abs ibib
```

L15 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STM  
 AB in the present experiment, 6-OHDA was infused directly into the  
 olfactory bulb  
 (OB) to produce a localized neurotoxic lesion.  
 Habituation/dishabituation  
 behavioral tests were then conducted to measure recognition responses to  
 chemical cues (urine as a stimulus) and to social stimuli  
 (ovariectomized rat  
 as a stimulus). Infusion of 6-OHDA resulted in a near complete depletion  
 of OB-norepinephrine (NE), whereas it had little effect (15% reduction)  
 on OB  
 dopamine (DA) contents. Nor were any significant effects on  
 hypothalamic,  
 hippocampal, olfactory tubercle, and corpus striatal NE and DA contents  
 observed Behaviorally, dishabituation responses to chemical cues were  
 greatly  
 impaired, however there was relatively little effect on social behavior  
 dishabituation responses. These results demonstrate that 6-OHDA can be  
 used to produce a near complete but localized depletion of OB-NE. This  
 treatment impairs dishabituation responses to chemical cues but not  
 social  
 stimuli indicating that OB-NE appears necessary for processing of  
 chemical  
 cue, but not social memory recognition process.  
 ACCESSION NUMBER: 1993:596325 CAPLUS  
 DOCUMENT NUMBER: 119:196325  
 TITLE: Depletion of olfactory bulb norepinephrine by 6-OHDA  
 disrupts chemical cue but not social recognition  
 responses in male rats  
 AUTHOR(S): Guan, Xiaobin; Blank, James; Dluzen, Dean  
 CORPORATE SOURCE: Department of Anatomy, Northeastern Ohio  
 Universities,  
 College of Medicine, Rootstown, OH, 44272, USA  
 SOURCE: Brain Research (1993), 622(1-2), 51-7  
 CODEN: BRREAP; ISSN: 0006-8993  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

=> d his

(FILE 'HOME' ENTERED AT 17:50:50 ON 06 DEC 2004)

FILE 'REGISTRY' ENTERED AT 17:50:54 ON 06 DEC 2004

L1 1 S ATOMOXETINE/CN

FILE 'CAPLUS' ENTERED AT 17:52:29 ON 06 DEC 2004

L2 50 S ATOMOX?

L3 50 S ATOMOXETINE

L4 107 S 83015-26-3/RN

L5 3 S 83015-26-3D/RN

L6 109 S L4 OR L5

L7 143300 S SEX?

L8 3 S L6 AND L7

L9 106 S L6 NOT L8

L10 131 S NOREPHINEPHRINE

L11 3 S L10 AND L7

L12 0 S "NOREPHINEPHRINE TRANSPORT INHIBITOR"

L13 11336 S NORADRENERGIC

L14 287 S L13 AND L7

L15 1 S L14 AND L10

=> s l10 not l11

L16 128 L10 NOT L11

=> d l16 1-128 abs ibib



L16 ANSWER 1 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The antidepressants, reboxetine and citalopram, were used in conjunction with voluntary phys. exercise (wheel running) in order to assess the contribution of noradrenergic and serotonergic activation to enhancements in hippocampal brain-derived neurotrophic factor (BDNF) expression resulting from antidepressant treatment and exercise. Reboxetine (40 mg/kg/day), citalopram (10 mg/kg/day), voluntary phys. activity, and the combination of antidepressants with exercise were applied to rats for a range of treatment intervals (2 to 14 days). Hippocampal BDNF transcription levels (full-length BDNF, as well as exons I-IV) were then assessed via in situ hybridization. Reboxetine treatment led to a rapid (evident at 2 days) enhancement in BDNF transcription in several hippocampal regions. This increase was also observed when reboxetine treatment was combined with voluntary phys. activity for 2 wk. Treatment with citalopram led to an increase in BDNF mRNA in only one hippocampal region (CA2) after short-term (2 days) treatment, and when combined with exercise, increased BDNF mRNA in the CA4 and dentate gyrus after 2 wk.

As reported in previous studies, voluntary phys. activity enhanced BDNF transcription in several hippocampal areas, both on its own and in combination with antidepressant treatments. Examination of the levels of individual BDNF transcript variants influenced by each of these antidepressants revealed distinct patterns of expression in response to the various treatments, and showed that exercise-plus-antidepressant produced significant changes where antidepressant alone failed. Overall, treatment with the norepinephrine-selective antidepressant, reboxetine, in combination with exercise, led to both rapid and sustained increases in hippocampal BDNF mRNA expression. The serotonergic agent, citalopram, appeared to require longer treatment intervals in order to influence BDNF expression pos. Neuropsychopharmacol. (2004) 29, 2189-2199, advance online publication, 16 June 2004.

ACCESSION NUMBER: 2004:1005087 CAPLUS  
 TITLE: Hippocampal Brain-Derived Neurotrophic Factor Expression Following Treatment with Reboxetine, Citalopram, and Physical Exercise  
 AUTHOR(S): Russo-Neustadt, Amelia A.; Alejandre, Hilda; Garcia, Celithelma; Ivy, Autumn S.; Chen, Michael J.  
 CORPORATE SOURCE: Department of Biological Sciences, California State University, Los Angeles, CA, USA  
 SOURCE: Neuropsychopharmacology (2004), 29(12), 2189-2199  
 CODEN: NROEOW; ISSN: 0893-133X  
 PUBLISHER: Nature Publishing Group  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 2 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB In August of 2001, the largest known installation of a phased temperature anaerobic process at a 60-MDG wastewater treatment plant was placed into operation. The facility met the time and temperature requirement for Class A biosolids. Testing of the biosolids following thermophillic/anaerobic digestion followed by mesophillic/anaerobic digestion revealed no detectable levels of fecal coliform bacteria in the treated biosolids. However, subsequent testing of the biosolids following dewatering by high solid centrifugation revealed high levels of fecal coliform bacteria. These biosolids, following high solid centrifugation, did not meet Class B requirements. This study indicated a very serious reactivation of fecal coliform bacteria following high solid centrifugation. Fifty-three percent of the fecal coliforms isolated were identified as Escherichia coli with two of the isolated organisms identified as E. coli O157:H7. E. coli O157:H7 has been shown to be capable of formation of an autoinducer in the presence of norepinephrine. The autoinducer triggers the growth of gram-neg. bacteria or the conversion of gram-neg. bacteria such as fecal coliforms from a non-culturable to culturable state. It is, therefore, hypothesized that the presence of E. coli O157:H7 may be involved in the reactivation of fecal coliform bacteria.

ACCESSION NUMBER: 2004:881666 CAPLUS  
 TITLE: Reactivation of fecal coliforms after anaerobic digestion and dewatering  
 AUTHOR(S): Hendrickson, Donald A.; Denard, Dave; Farrell, Joseph;  
 CORPORATE SOURCE: Higgins, Matt  
 SOURCE: Hoosier Microbiological Laboratory, Muncie, IN, 47303, USA  
 CONFERENCE: WEF/WEAU Residuals and Biosolids Management & Exhibition, 18th, Salt Lake City, UT, United States, Feb. 22-25, 2004 (2004), 908-916. Water Environment Federation: Alexandria, Va.  
 CODEN: 69FWM4  
 DOCUMENT TYPE: Conference; (computer optical disk)  
 LANGUAGE: English  
 REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L16 ANSWER 3 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Both diabetes (db/db) and obese (ob/ob) genotype mutations induce a hyperglycemic-hyperinsulinemic endometabolic state in C57BL mice, manifesting a type II NIDDM diabetes-obesity syndrome (DOS) in these leptin ligand/receptor-deficient models. The severity of the DOS induced by these single gene, homozygous-recessive mutations may be moderated by the background genome on which the mutation is expressed. The current studies define the phenotypic, systemic, cytochem. and cellular metabolic responses to db/db and ob/ob mutation expression when modified by /KsJ (severe DOS expression) or /6 (modified DOS expression) background strain influences as compared to littermate control (+/) indexes. Both db/db and ob/ob mutations induced dramatic increases in body wts., blood glucose and serum insulin concns. relative to +/- indexes when expressed on either the C57BL/KsJ (-/KsJ) or C57BL/6 (-/6) backgrounds. However, the -/KsJ background enhanced the severity of expression of these DOS indexes relative to the -/6 strain. Similarly, the -/KsJ genome suppressed cellular glucose uptake rates, pancreatic tissue wts. and insulin concns. in both db/db and ob/ob mutants relative to /6 background strain influences or +/- indexes. Concurrent enhancement of tissue and cellular lipogenic metabolism and islet cytolipid depositions were exaggerated when the mutations were expressed on the -/KsJ background relative to the -/6 genome. Pancreatic islet B-cell lipodeposition was markedly enhanced in ob/ob and db/db mutants expressed on either the -/KsJ or -/6 background. In both ob/ob and db/db models, B-cell insulin granulation was prominent in mildly hypertrophic pancreatic islets when the mutations were expressed on the -/6 background. In contrast, the severity of the DOS state expressed on the -/KsJ background resulted in pronounced B-cell atrophy, characterized by insulin degranulation, cellular hypertrophy and hypercytolipidemia associated with tissue involution, in both ob/ob and db/db mutants. Dramatic alterations in tissue norepinephrine (NE) and alpha-1-receptor populations in ob/ob and db/db mutants were exaggerated by the -/KsJ genome as compared to -/6 or control indexes. The influences of the -/KsJ genome on the progressive expression of tissue NE counter-regulatory responses to enhanced cytolipidemic indexes were inversely related, with cytochem. lipodeposition occurring under conditions of diminished adrenergic responses to the DOS indexes. The results of these studies indicate that the severity of the type-II diabetes endometabolic syndrome induced by the ob/ob or db/db genotypic mutations is modified by the existing genome on which the mutations are expressed. These data suggest that the severity of genomic mutation expression may be modified depending on the capability of the background genome to counter-regulate the systemic, cellular or metabolic consequences of these mutations.

ACCESSION NUMBER: 2004:805329 CAPLUS  
 TITLE: Cytochemical Analysis of Pancreatic Islet Hypercytolipidemia following Diabetes (db/db) and Obese (ob/ob) Mutation Expression: Influence of Genomic Background  
 AUTHOR(S): Garria, David R.; Garria, Bryan L.  
 CORPORATE SOURCE: Division of Cell Biology and Biophysics, Schools of Biological Sciences and Medicine, University of Missouri-Kansas City, Kansas City, MO, USA  
 SOURCE: Pathobiology (2004), 71(5), 231-240

L16 ANSWER 3 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
 CODEN: PATHEF; ISSN: 1015-2008  
 PUBLISHER: S. Karger AG  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L16 ANSWER 4 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
AB Cognitive dysfunction can be treated by administering to a mammal an effective amount of a compound that is an N-methyl-D-aspartate (NMDA) receptor antagonist and a selective norepinephrine (NE) serotonin (5-HT) reuptake inhibitor (NSRI), most preferably between 1:1 and 20:1 NE:5-HT reuptake. In a preferred embodiment the composition includes a pharmaceutically acceptable carrier and an effective cognition-enhancing amount of milnacipran, most preferably about 25 mg/day to about 250 mg/day. The composition may further include at least one of Ginkgo biloba, huperzine

A, phosphatidylserine, vitamin E, tacrine, donepezil, rivastigmine, and galantamine. The composition can also include at least one of sibutramine, an aminocyclopropane derivative, venlafaxine, duloxetine, desipramine, nortriptyline, protriptyline, amitriptyline, clomipramine, doxepine, imipramine, and trimipramine.

ACCESSION NUMBER: 2004:453075 CAPLUS  
DOCUMENT NUMBER: 140:417969  
TITLE: NMDA receptor antagonist-norepinephrine  
-serotonin reuptake inhibitor for the treatment of cognitive dysfunction, and use with other agents  
INVENTOR(S): Rao, Srinivas G.; Kranzler, Jay D.  
PATENT ASSIGNEE(S): Cypress Bioscience, Inc., USA  
SOURCE: PCT Int. Appl., 50 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO. | DATE       |
|------------------------|--|----------|-----------------|------------|
| WO 2004045718          | A2   | 20040603 | WO 2003-US36813 | 20031118   |
| WO 2004045718          | A3   | 20040812 |                 |            |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU |          |                 |            |
| RW:                    | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TH, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |            |
| PRIORITY APPLN. INFO.: |  |          | US 2002-42767P  | P 20021120 |
|                        |  |          | US 2003-443142P | P 20030128 |
|                        |  |          | US 2003-479761P | P 20030618 |

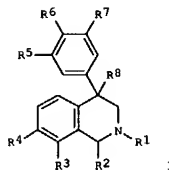
OTHER SOURCE(S): MARPAT 140:417969

L16 ANSWER 5 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)  
BR 2000015320 A 20020709 BR 2000-15320 20001103  
EP 1246806 A1 20021009 EP 2000-976985 20001103  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR  
JP 2003513074 T2 20030408 JP 2001-534777 20001103  
US 2002143014 A1 20021003 US 2002-91949 20020306  
US 6579885 B2 20030617  
US 2003203920 A1 20031030 US 2003-426097 20030429  
PRIORITY APPLN. INFO.:

|                 |    |          |
|-----------------|----|----------|
| US 1999-163269P | P  | 19991103 |
| US 2000-704305  | B1 | 20001102 |
| WO 2000-US30329 | W  | 20001103 |
| US 2002-91949   | A3 | 20020306 |

OTHER SOURCE(S): MARPAT 134:353258  
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L16 ANSWER 5 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
GI



AB Diaryl-methyltetrahydroisoquinolines (4R)- or (4S)-I [R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl; R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, haloalkyl; R3 = H, halogen, (un)substituted OH, S(O)H, CN, CHO, CONH2, alkyl, alkenyl, alkynyl, cycloalkyl; R4 = (un)substituted aryl, heteroaryl; R5-R7 = H, halogen, CN, (un)substituted OH, NH2, S(O)H, CHO, CONH2, alkyl, alkenyl, alkynyl, cycloalkyl; R8 = H, (un)substituted OH; n = 0-2] were prepared for use as blockers of the reuptake of norepinephrine, dopamine and serotonin (no data). Thus, 3-bromobenzaldehyde is stirred in the presence of methylamine and reduced with sodium borohydride followed by addition of  $\alpha$ -chloroacetophenone and reduction of the amino ketone in situ with sodium borohydride to give 3-BrC6H4CH2N(Me)CH2CH(OH)Ph; cyclization of the benzyl alc. with sulfuric acid followed by coupling with phenylboronic acid gave I (R1 = Me; R4 = Ph; R2 = R3 = R5 = R6 = R7 = H) as an oil. Such compds. are particularly useful in the treatment of a neuro. and psychiatric disorders which are created by or are dependent upon decreased availability of serotonin, norepinephrine or dopamine, such as attention deficit-hyperactivity disorder (ADHD), anxiety, depression, and addiction disorders.

ACCESSION NUMBER: 2001:338496 CAPLUS  
DOCUMENT NUMBER: 134:353258  
TITLE: Aryl- and heteroaryl-substituted tetrahydroisoquinolines and use thereof to block reuptake of norepinephrine, dopamine and serotonin  
INVENTOR(S): Beck, James P.; Curry, Matt A.; Smith, Mark A.  
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA  
SOURCE: PCT Int. Appl., 66 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE     |
|---------------|--|----------|-----------------|----------|
| WO 2001032625 | A1   | 20010510 | WO 2000-US30329 | 20001103 |
| W:            | AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR   |          |                 |          |
| CA 2389306    | AA   | 20010510 | CA 2000-2389306 | 20001103 |

L16 ANSWER 6 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
AB Background. Increased availability of norepinephrine (NE) for activation of cardiac adrenoceptors (increased cardiac adrenergic drive) and depletion of myocardial NE stores may contribute to the pathophysiol. and progression of congestive heart failure. This study used a comprehensive neurochem. approach to examine the mechanisms responsible for these abnormalities. Methods and Results. Subjects with and without congestive heart failure received i.v. infusions of [3H]NE. Cardiac spillover, reuptake, vesicular exchange, and tissue stores of NE were assessed from arterial and coronary venous plasma concns. of endogenous and [3H]-labeled NE and dihydroxyphenylglycol. Tyrosine hydroxylase activity was assessed from plasma dopa, and NE turnover was assessed from measurements of NE metabolites. NE release and reuptake were both increased in the failing heart; however, the efficiency of NE reuptake was reduced such that cardiac spillover of NE was increased disproportionately more than neuronal release of NE. Cardiac NE stores were 47% lower and the rate of vesicular leakage of NE was 42% lower in the failing than in the normal heart. Cardiac spillover of dopa and NE turnover were increased similarly in congestive heart failure. Conclusions. Increased neuronal release of NE and decreased efficiency of NE reuptake both contribute to increased cardiac adrenergic drive in congestive heart failure. Decreased vesicular leakage of NE, secondary to decreased myocardial stores of NE, limits the increase in cardiac NE turnover in CHF. Decreased NE store size in the failing heart appears to result not from insufficient tyrosine hydroxylation but from chronically increased NE turnover and reduced efficiency of NE reuptake and storage.

ACCESSION NUMBER: 1996:307880 CAPLUS  
DOCUMENT NUMBER: 125:7188  
TITLE: Cardiac sympathetic nerve function in congestive heart failure  
AUTHOR(S): Eisenhofer, Graeme; Friberg, Peter; Rundqvist, Bengt; Quyyumi, Arshed A.; Lambert, Gavin; Kaye, David M.; Kopin, Irwin J.; Goldstein, David S.; Esler, Murray D.  
CORPORATE SOURCE: National Institute Neurological Disorders and Stroke, National Institutes Health, Bethesda, MD, 20892-1424, USA  
SOURCE: Circulation (1996), 93(9), 1667-1676  
CODEN: CIRCZ; ISSN: 0009-7322  
PUBLISHER: American Heart Association  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 7 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The authors summarized behavioral and immunocytochem. results from rats with exptl. parkinsonism which were implanted with dopamine- or norepinephrine-containing microspheres. Implanted microspheres containing dopamine and norepinephrine attenuated apomorphine-induced rotational behavior in rats with chronic unilateral 6-hydroxydopamine lesions of the ascending (nigrostriatal) dopaminergic neurons. The catecholamine-containing microspheres also stimulated fiber growth in the striatum and fiber growth was related to functional recovery.

ACCESSION NUMBER: 1995:952644 CAPLUS  
 DOCUMENT NUMBER: 124:1284  
 TITLE: Catecholamine-containing biodegradable microsphere implants: An overview of experimental studies in dopamine-lesioned rats  
 AUTHOR(S): McRae, Amanda; Dahlstroem, Annica; Hjorth, Stephan; Ling, Eng Ang; Mason, David; Tice, Thomas  
 CORPORATE SOURCE: Department Anatomy, University Goteborg, Goeteborg, Swed.  
 SOURCE: Advances in Behavioral Biology (1995), 44(Alzheimers and Parkinsons Diseases), 421-7  
 CODEN: ADBBEW; ISSN: 0099-6246  
 PUBLISHER: Plenum  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 8 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A method was developed for detection of bromodeoxyuridine (BrdU) in conjunction with other antigens in formalin-fixed paraffin sections with microwave antigen retrieval. The method was applied to rat adrenal medulla to demonstrate S-phase nuclei in epinephrine-producing cells strained for immunoreactive phenylethanolamine-N-methyltransferase and in norepinephrine-producing cells stained for immunoreactive tyrosine hydroxylase. The quality for staining for all three antigens was comparable to or better than that previously obtained with other techniques. This method provides an efficient tool for studying turnover of subpopulations of adrenal chromaffin cells. It should also be widely applicable to other cells and tissues.

ACCESSION NUMBER: 1995:316663 CAPLUS  
 DOCUMENT NUMBER: 122:155579  
 TITLE: Triple immunohistochemical staining for bromodeoxyuridine and catecholamine biosynthetic enzymes using microwave antigen retrieval  
 AUTHOR(S): Tischler, Arthur S.  
 CORPORATE SOURCE: Department of Pathology, Tufts University School of Medicine, Boston, MA, USA  
 SOURCE: Journal of Histochemistry and Cytochemistry (1995), 43(1), 1-4  
 CODEN: JHCYAS; ISSN: 0022-1554  
 PUBLISHER: Histochemical Society, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 9 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB We have previously found that histamine H3-receptors are neg. coupled to norepinephrine exocytosis in atrial tissue. We report here that in the presence of H1- and H2-receptor blockers, histamine significantly inhibits the tachycardia and norepinephrine release elicited by sympathetic nerve stimulation in isolated guinea pig hearts, an effect prevented by the H3 antagonist, thioperamide. Sympathetic nerve stimulation also caused a 1.5-fold increase in histamine overflow, which was insufficient to activate H3 receptors because thioperamide affected neither the tachycardia nor the norepinephrine release. Hence, we questioned whether H3 receptors become activated when adrenergic activity is greatly enhanced, as in myocardial ischemia. Guinea pig hearts underwent 10-min global ischemia. At reperfusion, norepinephrine exocytosis was markedly augmented and was associated with a 3.5-fold increase in histamine overflow. (R)-methylhistamine, an H3 agonist, did not modify norepinephrine release, whereas thioperamide doubled it. Thus, in physiol. conditions, cardiac H3 receptors are quiescent, yet available for activation by exogenous ligands. In contrast, in the ischemic myocardium, H3 receptors appear to be fully activated by an endogenous ligand, probably histamine. Hence, cardiac H3 receptors may play an important role by neg. modulating exocytotic norepinephrine release associated with ischemic states.

ACCESSION NUMBER: 1995:273654 CAPLUS  
 DOCUMENT NUMBER: 122:78176  
 TITLE: Unmasking of activated histamine H3-receptors in myocardial ischemia: their role as regulators of exocytotic norepinephrine release  
 AUTHOR(S): Imamura, Michiaki; Poli, Enzo; Omoniyi, Abimbola T.; Levi, Roberto  
 CORPORATE SOURCE: Department of Pharmacology, Cornell University Medical College, New York, NY, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1994), 271(3), 1259-66  
 CODEN: JPETAB; ISSN: 0022-3565  
 PUBLISHER: Williams & Wilkins  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 10 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The authors hypothesized, first, that recent antecedent hypoglycemia causes reduced autonomic responses to subsequent hypoglycemia in patients with well-controlled insulin-dependent diabetes mellitus (IDDM) and that the reduced responses are specific for the stimulus of hypoglycemia while the responses to other stimuli are unaltered and, second, that reduced autonomic responses, specifically sympathochromaffin, so-induced are not simply the result of prior activation of the system. To test the first hypothesis, eight patients with IDDM, selected for HbA1c levels <8.0% and the absence of classic diabetic autonomic neuropathy, were studied twice. On one occasion, clamped hypoglycemia (.apprx.2.8 mM) was produced at 1400-1600 on days 2 and 3; on the other occasion clamped euglycemia (.apprx.5.6 mM) was produced at those times. On both occasions, autonomic responses to hypoglycemia (.apprx.2.8 mM) were determined the morning of day 3 and those to standing, exercise, and a formula meal the morning of day 4. Following afternoon hypoglycemia, 1) the adrenomedullary epinephrine (EPI) response to hypoglycemia was reduced (P = 0.0397) but that to standing, exercise, and a meal were unaltered; 2) the sympathetic neural norepinephrine (NE) response to standing and to exercise was unaltered; and 3) the partially parasympathetic neural-mediated pancreatic polypeptide response to a meal was unaltered.

ACCESSION NUMBER: 1994:505793 CAPLUS  
 DOCUMENT NUMBER: 121:105793  
 TITLE: Hypoglycemia-induced autonomic failure in IDDM is specific for stimulus of hypoglycemia and is not attributable to prior autonomic activation  
 AUTHOR(S): Rattarasarn, Chatchalit; Dagogo-Jack, Samuel; Zachwieja, Jeffery J.; Cryer, Philip E.  
 CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, USA  
 SOURCE: Diabetes (1994), 43(6), 809-18  
 CODEN: DIAE22; ISSN: 0012-1797  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 11 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The influence of a 1.75 g dose of ascorbic acid on subsequent 4-h urinary excretion of Ca and free dopamine, norepinephrine, and epinephrine was investigated in 38 young women. Small increases, relative to control values from the same subjects, were observed for both urinary Ca and urinary dopamine. No significant changes were observed in urinary norepinephrine, epinephrine, P, creatinine, volume, or pH. Stepwise multiple regression anal. was used to evaluate factors as predictors for the Ca in the control urine sample, the Ca in the urine sample following the ascorbic acid dose, and for the difference in Ca excretion in the 2 situations. In the equation predicting the difference in urinary Ca, difference in urinary dopamine was a highly significant factor,  $\mu\text{g}$  dopamine explaining 29% of the variance in mg Ca. Dopamine was also a significant factor in the equation for predicting Ca excretion in the ascorbic acid dose situation but was not significant in the control situation. These findings indicate some apparent effects of acute ascorbic acid administration and raise the question whether endogenous dopamine is involved in some aspect of Ca homeostasis.

ACCESSION NUMBER: 1993:58581 CAPLUS  
 DOCUMENT NUMBER: 116:58581  
 TITLE: Urinary excretion of calcium, dopamine, norepinephrine, and epinephrine in young women following ascorbic acid ingestion  
 AUTHOR(S): Long, Karen P.; Marcuson, Richard; Miyashita, Koichi; Tsao, Constance S.  
 CORPORATE SOURCE: Dep. Chem., Diablo Valley Coll., Pleasant Hill, CA, 94523, USA  
 SOURCE: Nutrition Research (New York, NY, United States) (1992), 12(9), 1051-63  
 CODEN: NTRSDC; ISSN: 0271-5317  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 12 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Epinephrine-producing cells are characterized by the presence of phenylethanolamine N-methyltransferase (PNMT), which catalyzes the formation of epinephrine from norepinephrine. A line of transgenic mice was generated which carry a chimeric gene containing human PNMT cDNA fused to the 4-kilobase fragment of the human dopamine  $\beta$ -hydroxylase (DBH) gene promoter, to switch catecholamine phenotype in the nervous and endocrine systems. Human PNMT transcripts and immunoreactivity were mainly detected in norepinephrine neurons in brain and sympathetic ganglion as well as in norepinephrine-producing cells in adrenal medulla of transgenic mice, indicating that the human DBH gene promoter of 4 kilobases is sufficient to direct expression of the gene in norepinephrine-producing cells. Anal. of catecholamines in the various tissues showed that the expression of human PNMT in transgenic mice induced the appearance of epinephrine in sympathetic ganglion and dramatic changes in norepinephrine and epinephrine levels in brain, adrenal gland, and blood. These results indicate that the addnl. PNMT expression in norepinephrine-producing cells can convert these cells to the epinephrine phenotype, and suggest that norepinephrine-producing cells normally possess the basic machinery required for the synthesis of epinephrine except for PNMT. Thus it appears that the only major difference between norepinephrine- and epinephrine-producing cells is the expression of PNMT.

The transgenic animals provide an expl. model to investigate the functional differences between norepinephrine and epinephrine.

ACCESSION NUMBER: 1992:228758 CAPLUS  
 DOCUMENT NUMBER: 116:228758  
 TITLE: Genetic alteration of catecholamine specificity in transgenic mice  
 AUTHOR(S): Kobayashi, Kazuto; Sasaoka, Toshikuni; Morita, Nagatsu, Ikuko; Iguchi, Akihisa; Kurosawa, Yoshikazu; Fujita, Keisuke; Nomura, Tatsuji; Kimura, Minoru; et al.  
 CORPORATE SOURCE: Sch. Med., Fujita Health Univ., Toyoake, 470-11, Japan  
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1992), 89(5), 1631-5  
 CODEN: PNASA6; ISSN: 0027-8424  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 13 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Rat brain cortex synaptosomes pre-incubated with [3H] norepinephrine were used (1) to provide evidence that part of the NMDA receptors mediating stimulation of norepinephrine (NE) release are located on the noradrenergic varicosities themselves, (2) to characterize these receptors and (3) to examine whether ethanol specifically inhibits the NMDA-evoked NE release via a presynaptic site of action. In synaptosomes superfused with  $\text{Mg}^{2+}$ -free Krebs-Henseleit solution, NMDA (2-min exposure) stimulated tritium overflow in a concentration- and glycine-dependent manner. The stimulatory effect of NMDA was not altered by tetrodotoxin but was abolished by omission of  $\text{Ca}^{2+}$  from the superfusion fluid and was considerably reduced in the presence of 1.2 mM  $\text{Mg}^{2+}$ . DL-(E)-2-Amino-4-methyl-5-phosphono-3-pentanoic acid (CGP 37849; a competitive NMDA receptor antagonist) produced a parallel shift of the concentration-response curve for NMDA to the right, whereas dizocilpine (MK-801; an antagonist at the phencyclidine, PCP, recognition site of the NMDA-gated ion channel) reduced the maximum effect of NMDA. Ethanol inhibited the NMDA-evoked tritium overflow in a concentration-dependent manner. In contrast, in synaptosomes superfused with  $\text{Ca}^{2+}$ -free Krebs-Henseleit solution containing 15 mM  $\text{K}^{+}$  throughout, ethanol did not affect the tritium overflow evoked by 2 min introduction of 75  $\mu\text{M}$   $\text{Ca}^{2+}$  into the superfusion fluid. This  $\text{Ca}^{2+}$ -evoked overflow was also not altered by tetrodotoxin and dizocilpine, but was inhibited by the inorg.  $\text{Ca}^{2+}$  channel antagonist  $\text{Cd}^{2+}$ . Therefore, (1) NMDA receptors mediating stimulation of NE release are also located on the cortical noradrenergic varicosities (and not only on so far unknown excitatory interneurons within the cortex); (2) these receptors exhibit the characteristic pharmacol. features of the NMDA receptor system; (3) ethanol selectively inhibits the NE release evoked by stimulation of the presynaptic NMDA receptors, leaving the  $\text{Ca}^{2+}$ -evoked release promoted by high  $\text{K}^{+}$  unaffected. This finding is compatible with the suggestions that the NMDA receptor system itself is a site of action of ethanol.

ACCESSION NUMBER: 1992:168219 CAPLUS  
 DOCUMENT NUMBER: 116:168219  
 TITLE: Presynaptic site of action underlying the ethanol-induced inhibition of norepinephrine release evoked by stimulation of N-methyl-D-aspartate (NMDA) receptors in rat cerebral cortex  
 AUTHOR(S): Pink, Klaus; Goethert, Manfred  
 CORPORATE SOURCE: Inst. Pharmacol. Toxicol., Univ. Bonn, Bonn, D-5300, Germany  
 SOURCE: Brain Research (1992), 572(1-2), 27-32  
 CODEN: BRREAP; ISSN: 0006-8993  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 14 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Effects of norepinephrine (NE, 10-6 M), epinephrine (E, 10-6 M), and vehicle on coronary blood flow (CF), oxygen consumption, and lactate release were compared in 32 isolated rat hearts during 5 min of ventricular fibrillation (VF). After VF, tissue concns. of ATP, AMP, creatinine phosphate (CP), and lactate were measured. Perfusion of treatments started 30 s after onset of VF and was maintained throughout VF. CF during VF was greater during perfusion of E (5.73 mL/min) than NE (5.06 mL/min) or vehicle (5.11 mL/min). Oxygen consumption during VF was higher during perfusion of E (29.5  $\mu\text{L}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$  wet heart wt-1) than vehicle (27.3  $\mu\text{L}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ); average oxygen consumption during NE (27.6  $\mu\text{L}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ) and vehicle were comparable. After NE, but not E, tissue AMP concns. were increased; and CP concns. were reduced compared with vehicle. Enhanced consumption of high-energy phosphates during NE suggests that there is also an enhanced demand for oxygen. However, unlike during E, during NE this demand is not met by an augmented CF. Thus, compared with E, NE treatment during VF may increase the risk of hypoxic damage.

ACCESSION NUMBER: 1992:19115 CAPLUS  
 DOCUMENT NUMBER: 116:19115  
 TITLE: Adrenergic influences on cardiac function during ventricular fibrillation in isolated rat hearts  
 AUTHOR(S): Derad, I.; Funk, I.; Pauschinger, P.; Born, J.  
 CORPORATE SOURCE: Univ. Ulm, Ulm, 7900, Germany  
 SOURCE: American Journal of Physiology (1991), 261(5, Pt. 2), H1452-6  
 CODEN: AJPHAP; ISSN: 0002-9513  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 15 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB This study was carried out to investigate the possibility of local epinephrine (E) synthesis in rat cardiac tissue and to study the effect of bilateral adrenalectomy (A EX) on catecholamine synthesis. Bilateral adrenalectomy reduced cardiac and plasma E levels, but a substantial amount of E (33.3%) was retained in the atrium 9 days after bilateral adrenalectomy. There were also redns. in atrial norepinephrine (NE) and dopamine (DA) as well as ventricular DA. Cardiac E-forming activity (EFA) was not affected in ADX rats, but ventricular EFA showed a 42.3% increase compared to sham operated (SH) rats. Cardiac dopamine  $\beta$ -hydroxylase (DBH) activity was increased in the atrium (31%) and in the ventricle (60%) of ADX rats compared to SH rats. In SH rats, decapitation increased plasma E 61-fold but lowered plasma DA levels compared to the corresponding rest values, indicating that plasma DA is incorporated in the synthesis of catecholamines in the adrenal medulla. Thus, cardiac tissue synthesizes its own E and bilateral adrenalectomy increases sympathetic activity, catecholamine synthesis, and NE turnover.

ACCESSION NUMBER: 1991:624423 CAPLUS  
 DOCUMENT NUMBER: 115:224423  
 TITLE: Effect of bilateral adrenalectomy on catecholamine synthesis in the rat heart  
 AUTHOR(S): Elayan, Hamzeh H.; Gharaibeh, Munir N.  
 CORPORATE SOURCE: Fac. Med., Univ. Leeds, UK  
 SOURCE: Dirasat - University of Jordan (1989), 16(4), 115-29  
 CODEN: DUJGES; ISSN: 0255-8033  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 16 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB This study investigated the effects of iontophoretic application of excitatory amino acid (EAA) and norepinephrine (NE) agonists and antagonists on synaptic transmission to individual jaw-opener motoneurons (digastric) during activation of the jaw-opening reflex (JOR) evoked by stimulation of either fibers within the oral mucosa (OM) or tooth-pulp (TP). During both OM and TP stimulation, kynurenic acid (KYN), a wide-spectrum EAA antagonist, suppressed jaw-opener motoneuron discharge. Application of DL-2-amino-5-phosphonvaleric acid (APV), an NMDA receptor antagonist, also suppressed motoneuron discharge evoked by TP stimulation, but produced minimal effects on motoneuron discharge evoked by OM stimulation. These data suggest a role of EAA in mediating synaptic transmission from last-order interneurons to jaw-opener motoneurons during the jaw-opening reflex evoked by intra-oral stimulation. Iontophoretic application of NE produced dual effects (facilitation or suppression) on motoneuron discharge evoked by OM or TP stimulation. The effects were not related to the mode of motoneuronal activation. Iontophoretic application of the  $\alpha 1$  agonist, phenylephrine, facilitated motoneuronal discharge. In contrast, application of the  $\alpha 2$  agonist, clonidine, suppressed motoneuronal discharge during intra-oral stimulation. These effects were antagonized by prior iontophoretic application of the  $\alpha 1$  antagonist, prazosin, or the  $\alpha 2$  antagonist, yohimbine, resp. In those cells in which the predominant effect of NE application on synaptic transmission was either facilitation or suppression of motoneuronal discharge, prior iontophoretic application of prazosin or yohimbine, resp., antagonized the effects of NE application. These data suggest that NE can modulate synaptic transmission to jaw-opener motoneurons evoked by intra-oral stimulation via activation of  $\alpha 1$  or  $\alpha 2$  adrenoreceptors on trigeminal motoneurons.

ACCESSION NUMBER: 1991:528119 CAPLUS  
 DOCUMENT NUMBER: 115:128119  
 TITLE: Iontophoretic analysis of the pharmacologic mechanisms responsible for initiation and modulation of trigeminal motoneuronal discharge evoked by intra-oral afferent stimulation  
 AUTHOR(S): Katakura, Nobuo; Chandler, Scott H.  
 CORPORATE SOURCE: Brain Res. Inst., Univ. California, Los Angeles, CA, 90024, USA  
 SOURCE: Brain Research (1991), 549(1), 66-77  
 CODEN: BRREAP; ISSN: 0006-8993  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 17 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB To define the role of norepinephrine regulation of growth hormone (GH) secretion in a primate species, spontaneous and GH-releasing hormone (GHRH) stimulated GH secretion was studied in 6 chronically catheterized adult male cynomolgus monkeys before and after inhibition of norepinephrine synthesis. Blood samples were obtained at 15-min intervals over 8 h to characterize the pattern of GH secretion, and the GH response to GHRH (10  $\mu$ g/kg, i.v.) was determined. These measurements were repeated 2 wk later, 2 h after the i.v. administration of 12.5 mg/kg of the dopamine  $\beta$ -hydroxylase inhibitor diethylthiocarbamate (DDTC), which has been shown to be effective norepinephrine synthesis inhibitor in the rat. Spontaneous and stimulated GH secretory patterns before and after DDTC administration were compared. Both the frequency and the amplitude of spontaneous GH pulses were markedly reduced by DDTC (3.8 before vs. 1.8 peaks/8 h after DDTC and 5.5 vs. 2.0 ng/mL). Areas under the curve were also reduced by DDTC treatment (10.8 vs. 5.7 ng  $\cdot$  h/mL), and DDTC administration diminished the peak GH responses to GHRH (12 vs. 4 ng/mL). These results are consistent with the belief that DDTC is a potent inhibitor of spontaneous and GHRH-induced GH secretion. The action of DDTC could be mediated by a reduction in GHRH due to reduced norepinephrine synthesis, by an increase in somatostatin release through a dopaminergic stimulus, or by a direct dopaminergic effect on somatotrophs.

ACCESSION NUMBER: 1990:112436 CAPLUS  
 DOCUMENT NUMBER: 112:112436  
 TITLE: Effects of inhibition of norepinephrine synthesis on spontaneous and growth hormone-releasing hormone-induced GH secretion in cynomolgus macaques: evidence for increased hypothalamic somatostatin tone  
 AUTHOR(S): Malozowski, Saul; Hao, En Hui; Ren, Song Guang; Genazzani, Alessandro D.; Kalogeras, Konstantine T.; Merriam, George R.  
 CORPORATE SOURCE: Dev. Endocrinol. Branch, Natl. Inst. Child Health and Hum. Dev., Bethesda, MD, 20892, USA  
 SOURCE: Neuroendocrinology (1990), 51(4), 455-8  
 CODEN: NUNDAJ; ISSN: 0028-3835  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 18 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB To investigate the possible involvement of pp60c-src in exocytosis, cultured bovine chromaffin cells were analyzed for changes in c-src tyrosine kinase activity in response to stimulation by several secretagogues. Results of in vitro immune complex kinase assays showed that pp60c-src, derived from cells that had been stimulated for various lengths of time, exhibited decreased auto- and transphosphorylating activities as compared to pp60c-src immunopptd. from control cells. The greatest reduction in activity was observed 10 min post-stimulation, whereas normal levels were regained 2-6 g after secretagogue treatment. Western immunoblot anal. of the immunopptd. pp60c-src revealed that .apprx.50% less c-src protein was present in immune complexes prepared 10 min after stimulation as compared to those prepared from mock-stimulated controls, resulting in a specific autophosphorylating activity that was 42-47% of control and little or no reduction in the transphosphorylating specific activity. In expts. in which the rate of secretion of [3H]norepinephrine from cells preloaded with this compound was compared to the rate of modulation of pp60c-src activity, 50% of the maximal reduction in pp60c-src activity occurred within 2-4 min, whereas 50% maximal release of [3H] norepinephrine occurred within 1-3 min. Apparently, pp60c-src may play some role (direct or indirect) in the exocytotic process.

ACCESSION NUMBER: 1989:612420 CAPLUS  
 DOCUMENT NUMBER: 111:212420  
 TITLE: Modulation of pp60c-src tyrosine kinase activity during secretion in stimulated bovine adrenal chromaffin cells  
 AUTHOR(S): Oddie, K. M.; Litz, J. S.; Balserak, J. C.; Payne, D. M.; Creutz, C. E.; Parsons, Sarah J.  
 CORPORATE SOURCE: Sch. Med., Univ. Virginia, Charlottesville, VA, 22908, USA  
 SOURCE: Journal of Neuroscience Research (1989), 24(1), 38-48  
 CODEN: JNREDA; ISSN: 0360-4012  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 19 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Repetitive peer sepn. of rhesus monkeys was used to study oxaprotiline effects on various components of the depressive syndrome. This paradigm is sensitive to norepinephrine. Oxaprotiline, a norepinephrine uptake inhibitor, showed results in less severe behavioral reactions to social separation CGP12103A, the (-)-isomer of oxaprotiline, which has no effect on norepinephrine, should have no effect on the paradigm. However, both isomers caused alterations in certain components of the behavioral response to separation (stereotypy, huddling, locomotion, self-directed behavior and inactivity) and specifically caused a reduction in stereotypic behaviors.

ACCESSION NUMBER: 1989:185800 CAPLUS  
 DOCUMENT NUMBER: 110:185800  
 TITLE: Effects of oxaprotiline on the response to peer separation in rhesus monkeys  
 AUTHOR(S): McKinney, William T.; Kraemer, Gary W.  
 CORPORATE SOURCE: Sch. Med., Univ. Wisconsin, Madison, WI, USA  
 SOURCE: Biological Psychiatry (1989), 25(6), 818-21  
 CODEN: BIPCBF; ISSN: 0006-3223  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 20 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Differential effects of 2 calmodulin antagonists, W-7 and W-5, on synapsin I phosphorylation and norepinephrine release associated with Ca2+ influx, were investigated using [32P]phosphate in synaptosomes derived from rat cerebral cortex. The Ca2+ ionophore (A23187)-stimulatory effect on synapsin I phosphorylation and norepinephrine release was markedly reduced by W-7 and slightly reduced by W-5, whereas neither the strong nor the weak calmodulin antagonist had an effect on A23187-stimulated synaptosomal uptake of Ca2+. Preincubation with H-8 reduced both W-5- and W-7-inhibited A23187-stimulated synapsin I phosphorylation by the same amount but did not affect their inhibitory effect nor the ionophore-stimulated norepinephrine release, thereby suggesting that W-5 may serve as an appropriate control for the noncalmodulin-mediated effect of both calmodulin antagonists.

ACCESSION NUMBER: 1989:53099 CAPLUS  
 DOCUMENT NUMBER: 110:53099  
 TITLE: Clearer demonstration of calcium/calmodulin-dependent events in synaptosomes by use of the differential effects of two calmodulin antagonists, N-(aminohexyl)-5-chloro-1-naphthalenesulfonamide and N-(6-aminohexyl)-1-naphthalenesulfonamide  
 AUTHOR(S): Imai, Shizuko; Onozuka, Minoru  
 CORPORATE SOURCE: Sch. Med., Gifu Univ., Gifu, 500, Japan  
 SOURCE: Comparative Biochemistry and Physiology, Part C: Pharmacology, Toxicology & Endocrinology (1988), 91C(2), 535-40  
 CODEN: CBPCEE; ISSN: 0742-8413  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 21 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Nerve degeneration techniques (ganglionectomy, interganglionic secretion, postganglionic axotomy, uni- or bilateral hypogastric nerve section, and right pelvic ganglionectomy) and fluorometric detns. of histamine and norepinephrine showed the presence of nervous pathways containing histamine adjacent to the sympathetic system of the rat vas deferens. Apparently, these pathways cross between the ganglionic clusters located at the angle formed by the seminal vesicle and the vas deferens. They are not structurally related to the central nervous system by way of the hypogastric or pelvic ganglion. The histamine-containing pathways were independent of the noradrenergic pathways, as dissociation between norepinephrine depletion and histamine depletion was shown under nerve degeneration. The time course of nerve degeneration over a long period after sympathectomy showed a biphasic effect on histamine levels of the vas deferens. The early histamine depletion was indicative of degeneration of histamine-containing pathways, and the delayed histamine increasing phase was considered to be due to the accumulation of mast cells in the degenerating nerve sheaths. A possible role for the histamine-containing pathways in the modulation of sympathetic activity is envisaged.

ACCESSION NUMBER: 1988:180681 CAPLUS  
 DOCUMENT NUMBER: 108:180681  
 TITLE: A possible crossed histamine-containing pathway adjacent to the sympathetic system of the rat vas deferens  
 AUTHOR(S): Campos, H. Augusto  
 CORPORATE SOURCE: Vargas Med. Sch., Cent. Univ. Venezuela, Caracas, 1070-A, Venez.  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1988), 244(3), 1121-7  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 22 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The effect of dihydroxyphenylacetic acid (DOPAC), the 1st deaminated metabolite of dopamine (DA), on norepinephrine (NE) accumulation in the brain after s.c. L-dopa treatment was studied in rats. Intracerebroventricular injection of DOPAC before or after L-dopa treatment had no effect on DA and NE concns. in the rat brain. In rats pretreated with pargyline, a DA deamination inhibitor, and injected with L-dopa, high concns. of DOPAC did not restrict NE accumulation.

ACCESSION NUMBER: 1988:179968 CAPLUS  
 DOCUMENT NUMBER: 108:179968  
 TITLE: Effect of intraventricular injections of 3,4-dihydroxyphenylacetic acid (DOPAC) on cerebral norepinephrine accumulation in L-dopa treated rats  
 AUTHOR(S): Boudet, C.; Buu, N. T.; Duhaime, J.; Kuchel, O.; Peyrin, L.  
 CORPORATE SOURCE: Lab. Physiol., Fac. Med. Grange-Blanche, Lyon, 69373, Fr.  
 SOURCE: Biogenic Amines (1987), 4(4-6), 413-17  
 CODEN: BIAME7; ISSN: 0168-8561  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

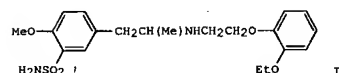
L16 ANSWER 23 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The vascular responses to acetylcholine (ACh), norepinephrine (NE), KCl, and diltiazem were examined before and after removal of endothelial cells by an intraluminal bolus injection of saponin (1 mg) in isolated and perfused dog coronary arteries. Without any precontraction, ACh induced a long-lasting vasodilation in small doses (<1 µg), and an initial brief vasoconstriction was occasionally accompanied in large doses. These vascular responses to ACh were not significantly affected by the pretreatment with propranolol (5 × 10<sup>-6</sup> mol/L). The endothelial removal by intraluminal saponin was confirmed electron microscopically. After 20-60 min of saponin treatment, the ACh-induced vasodilation was significantly attenuated by saponin, but the ACh-induced vasoconstriction was not affected by it. The vasodilation was blocked by atropine. The NE- and KCl-induced vasoconstrictions and diltiazem-induced vasodilation were not affected by saponin treatment. Thus ACh produced a vasodilation in the nonprecontracted condition of dog coronary arteries, the vasodilation caused by ACh is mostly endothelium-dependent and considered to be mediated by muscarinic receptors, and the vascular responses to NE, KCl, and diltiazem and the vasoconstriction produced by ACh are not influenced by removal of the endothelium in a relatively large epicardial coronary artery of the dog.

ACCESSION NUMBER: 1987:452624 CAPLUS  
 DOCUMENT NUMBER: 107:52624  
 TITLE: Responses of isolated and perfused dog coronary arteries to acetylcholine, norepinephrine, potassium chloride, and diltiazem before and after removal of the endothelial cells by saponin  
 AUTHOR(S): Nakane, Tokio; Ito, Nobuo; Chiba, Shigetoshi  
 CORPORATE SOURCE: Sch. Med., Shinshu Univ., Matsumoto, 390, Japan  
 SOURCE: Heart and Vessels (1986), 2(4), 221-7  
 CODEN: HEVEEO; ISSN: 0910-8327  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 24 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The recovery of plasma glucose and the responses of counterregulatory hormone after insulin-induced hypoglycemia were investigated in 7 normal controls and 16 non-insulin-dependent diabetic patients (NIDDM). Seven of the diabetics (group A) had no autonomic neuropathy, and 9 (group B) had autonomic neuropathy. There were no differences in the rate of plasma glucose decrement and the nadir glucose concentration in the 3 groups. The incremental areas of plasma glucose concentration from 15 (glucose nadir) to 90 min were 2267, 2132, and 874 mg/min/dL in controls and groups A and B, resp. The increment in group B was lower than in the other groups. The incremental areas of each hormone from 0 to 90 min after the end of insulin infusion were calculated. EA Glucagon (IRG) in controls and groups A and B was 2210, 2369, and 762 pg/min/mL, resp. The EAIRG in group B was lower than that in group A. EA Epinephrine (PE) was 4.95 ng/min/mL in controls, 6.89 in group A, and 3.04 in group B. EAPE in group B was lower compared with that in group A. EA Norepinephrine (PNE) in controls and groups A and B was, 3.36, 4.05, and 1.83 ng/min/mL, resp. EA PNE in group B was lower than in the others. There were no differences in EA growth hormone and EA cortisol in the 3 groups. The glucose recovery and the increments of counterregulatory hormone were similar in the controls and the NIDDM patients without autonomic neuropathy, whereas the glucose recovery was delayed in the NIDDM patients with autonomic neuropathy due to reduced secretion of glucagon and catecholamines. Heart rate variations in the groups are described. Apparently, autonomic nervous activity is of major importance for counterregulatory hormone secretion after hypoglycemia in NIDDM patients. Whether NIDDM patients, if treated strictly with insulin, have an increased risk for hypoglycemia must be assessed in advance by testing autonomic function.

ACCESSION NUMBER: 1986:107310 CAPLUS  
 DOCUMENT NUMBER: 104:107310  
 TITLE: Quantitative evaluation of diabetic autonomic neuropathy based on heart rate variations - Relationship between autonomic neuropathy and counterregulatory hormone secretion after hypoglycemia  
 AUTHOR(S): in non-insulin-dependent diabetic patients  
 Oikawa, Noboru; Sanoyama, Kyo; Abe, Ryuzo; Sato, Hideyuki; Sakurada, Mikio; Toyota, Takayoshi; Goto, Yoshio  
 CORPORATE SOURCE: Sch. Med., Tohoku Univ., Sendai, Japan  
 SOURCE: Tonyobyo (Tokyo, Japan) (1985), 28(9), 1073-9  
 CODEN: TONYA4; ISSN: 0021-437X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Japanese

L16 ANSWER 25 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB The effects of YM-12617 (I) [80223-99-0] on the electrophysiol. properties of smooth muscle membranes and prejunctional nerve terminals and contractions evoked by different procedures were studied using guinea pig mesenteric and pulmonary arteries. I (> 1nM) inhibited the depolarization induced by norepinephrine in both muscle tissues. Yohimbine had no effect, whereas prazosin inhibited the norepinephrine-induced depolarization to a lesser extent than I. When I (> 1nM) was applied to the mesenteric artery, the amplitude of the 1st excitatory-junction potential evoked by a train stimulation of perivascular nerves was inhibited, but the facilitation of excitatory-junction potentials evoked by frequencies over 0.1 Hz was enhanced. As a consequence, the amplitude of the excitatory junction potentials after completion of the facilitation exceeded the control, as was expected to occur with a typical α2-adrenoceptor blocker. I inhibited the contraction evoked by exogenously applied norepinephrine or perivascular nerve stimulation, with a higher potency than seen with prazosin, but this agent had no effect on the contraction evoked by excess concns. of K<sup>+</sup> or by direct muscle stimulation. Apparently, I possesses a more potent α1-adrenoceptor blocking action than does prazosin, and is more selective for α1- than for α2-adrenoceptors.

ACCESSION NUMBER: 1986:102335 CAPLUS  
 DOCUMENT NUMBER: 104:102335  
 TITLE: Effects of YM-12617, an alpha adrenoceptor blocking agent, on electrical and mechanical properties of the guinea pig mesenteric and pulmonary arteries  
 AUTHOR(S): Fujii, Koji; Kuriyama, Hiroshi  
 CORPORATE SOURCE: Fac. Med., Kyushu Univ., Fukuoka, 812, Japan  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1985), 235(3), 764-70  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

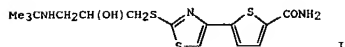
L16 ANSWER 26 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Adrenal secretion rates and arterial plasma epinephrine (E) [51-43-4], norepinephrine (NE) [51-41-2], and dopamine [51-61-6] levels were studied in 9 groups of mongrel dogs under pentobarbital anesthesia: (1) resting animals; (2) hemorrhage (25 mL/kg); (3) hemorrhage after acute nephrectomy; (4-7) hemorrhage and acute nephrectomy and i.v. angiotensin II [11128-99-7] at 0.01, 0.10, 1.00, or 10.00 ng/kg/min; (8) no hemorrhage, acute nephrectomy, angiotensin II (10.00 ng/kg/min); and (9) hemorrhage, kidneys intact, i.v. angiotensin II (10.00 ng/kg/min). Arterial and adrenal blood were sampled during a baseline prehemorrhage period and 15, 30, 60, and 90 min after hemorrhage. Results confirmed blunting of reflex E release by acute nephrectomy in the anesthetized dog and showed that angiotensin II restores E, NE, and dopamine release in acutely anephric dogs. Aortic plasma E and NE were also restored to normal by angiotensin II. Dogs with intact kidneys show a blunted hemorrhage response of arterial plasma E, NE, and dopamine to the largest angiotensin II infusion rate (10 ng/kg/min). Apparently, in acutely anephric conditions, angiotensin II support of reflex catecholamine release is sensitively dose dependent to physiol. infusion rates of systemic angiotensin II and this angiotensin II effect is restrained by the kidney.

ACCESSION NUMBER: 1985:607552 CAPLUS  
 DOCUMENT NUMBER: 103:207552  
 TITLE: Angiotensin II restoration of reflex adrenal medullary secretion to anephric dogs is physiologically dose dependent  
 AUTHOR(S): Badder, Elliott M.; Duarte, Bernardo; Seaton, John F.; Hamaji, Masayasu; Harrison, Timothy S.  
 CORPORATE SOURCE: Med. Sch., Univ. Maryland, Baltimore, MD, 21201, USA  
 SOURCE: Endocrinology (1985), 117(5), 1920-9  
 CODEN: ENDOAO; ISSN: 0013-7227  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 27 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A series of studies were performed to determine the relationship between  
 physiol. levels of circulating plasma norepinephrine [51-41-2] and  
 epinephrine [51-43-4] and human platelet alpha-2 binding site number  
 and the  
 affinity (KD) of these sites for antagonist radioligands. In one study,  
 alpha-2-adrenergic binding site number and affinity were compared using  
 both  
 3H-labeled yohimbine [146-48-5] and 3H-labeled dihydroergocryptine  
 [25447-66-9] as radioligands. There was good absolute and relative  
 comparison  
 for binding site number, but only a relative relationship for KD. In 46  
 normal subjects, there was no significant relationship between site  
 number or  
 KD and age, plasma epinephrine, or plasma norepinephrine concentration  
 Even  
 after plasma epinephrine was raised nearly 20-fold by means of an i.v.  
 infusion for 4 h in 7 normal subjects, neither sites (608 vs. 567  
 sites/platelet) nor KD (2.01 vs. 2.14 nM) were significantly changed.  
 Similarly, neither sites (445 vs. 421 sites/platelet) nor KD (1.44 vs.  
 2.10 nM) were significantly changed in 6 normal subjects when plasma  
 norepinephrine levels increased during oral administration of  
 prazosin for 1 wk. Thus, in a cross-sectional anal. and after a change  
 in  
 plasma catecholamine concns., there was no relationship in normal  
 subjects  
 between platelet alpha-2 binding site number or affinity of these sites  
 for  
 antagonist radioligands and the circulating catecholamine levels to which  
 the platelets were exposed.  
 ACCESSION NUMBER: 1984:583886 CAPLUS  
 DOCUMENT NUMBER: 101:183886  
 TITLE: Variations in circulating catecholamines fail to  
 alter  
 human platelet alpha-2-adrenergic receptor number or  
 affinity for [3H]yohimbine or [3H]dihydroergocryptine  
 AUTHOR(S): Pfeifer, M. A.; Ward, K.; Malpass, T.; Stratton, J.;  
 Halter, J.; Evans, M.; Belter, H.; Harker, L. A.;  
 Porte, D., Jr.  
 CORPORATE SOURCE: Univ. Washington, Seattle, WA, USA  
 SOURCE: Journal of Clinical Investigation (1984), 74(3),  
 1063-72  
 CODEN: JCINAO; ISSN: 0021-9738  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 28 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Pineal tryptophan [73-22-3], serotonin [50-67-9], serotonin-N-  
 acetyltransferase (NAT) [9027-33-2], melatonin [73-31-4],  
 5-hydroxyindoleacetic acid [54-16-0], norepinephrine [51-41-2] and  
 dopamine [51-61-6] were measured in castrated rabbits at 11.00, 00.30,  
 and 03.00 h. The rabbits were housed in a light:dark 14:10 (lights on  
 07.00 h). Significant day:night variations were found in NAT, melatonin,  
 dopamine, and norepinephrine. These results were compared to data on  
 rhythms of pineal constituents in other species.  
 ACCESSION NUMBER: 1984:564206 CAPLUS  
 DOCUMENT NUMBER: 101:164206  
 TITLE: Day:night variations of melatonin,  
 5-hydroxyindoleacetic acid, serotonin, serotonin  
 N-acetyltransferase, tryptophan,  
 norepinephrine and dopamine in the rabbit  
 pineal gland  
 AUTHOR(S): Brainard, George C.; Matthews, Susan A.; Steger,  
 Richard W.; Reiter, Russel J.; Asch, Ricardo H.  
 CORPORATE SOURCE: Dep. Neurol., Jefferson Med. Coll., Philadelphia, PA,  
 19107, USA  
 SOURCE: Life Sciences (1984), 35(15), 1615-22  
 CODEN: LIFSAK; ISSN: 0024-3205  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 29 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB The effects of arotinolol (I) [68377-92-4] on dog coronary arteries were  
 investigated in vitro. In distal portions of left circumflex coronary  
 arteries contracted with 3 + 10-2 M KCl, norepinephrine  
 [51-41-2] relaxed the strips in a concentration-dependent fashion.  
 Propranolol  
 [525-66-6] (10-6 M) converted the norepinephrine-induced relaxations to  
 contractions, and arotinolol (10-6-10-5 M) inhibited the relaxations  
 induced by norepinephrine in a concentration-dependent manner. In  
 proximal  
 portions of the strips after K+ contracture, norepinephrine  
 produced concentration-dependent contractions which were augmented by  
 propranolol  
 (10-6 M) and inhibited by arotinolol (10-6-10-5 M). This suggested that  
 arotinolol has an alpha-adrenoceptor blocking activity in addition to a  
 beta-adrenoceptor blocking action in dog coronary arteries.  
 ACCESSION NUMBER: 1984:503903 CAPLUS  
 DOCUMENT NUMBER: 101:103903  
 TITLE: Possible alpha-adrenoceptor blocking activity of  
 arotinolol (S-596), a new beta-adrenoceptor blocking  
 agent in isolated dog coronary artery  
 AUTHOR(S): Sakanashi, Matao; Miyamoto, Yoshimasa; Ito, Hirosumi;  
 Takeo, Satoshi; Noguchi, Katsuhiko; Higa, Tomoyo  
 CORPORATE SOURCE: Fac. Med., Univ. Ryukyus, Okinawa, Japan  
 SOURCE: Pharmacology (1984), 29(4), 204-9  
 CODEN: PHMGBN; ISSN: 0031-7012  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

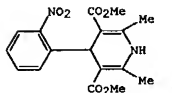
L16 ANSWER 30 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Tracer-labeled l-[3H]-norepinephrine, d-[14C]norepinephrine,  
 and d,l-[3H]-isoproterenol were infused simultaneously into patients with  
 essential hypertension and into normotensive control subjects, in order  
 to  
 determine whether abnormalities in the disappearance kinetics of these  
 substances characterized the hypertensive patients. The mean preinfusion  
 venous plasma norepinephrine concentration was somewhat higher in the  
 hypertensive group (260 vs. 194 pg/mL), but the groups did not differ in  
 the disappearance kinetics of l- or d-norepinephrine or of isoproterenol.  
 Preinfusion plasma norepinephrine was significantly pos. correlated with  
 calculated spillover rates in both the hypertensive and normotensive  
 groups,  
 but not with norepinephrine clearances. The d/l ratio in plasma  
 norepinephrine was the same as in the infusate during and after the  
 infusion, even after pretreatment with the neuronal norepinephrine uptake  
 blocker, desipramine. Because isoproterenol is not taken up by nerve  
 endings, the ratio of [3H]isoproterenol to l-[3H]norepinephrine increased  
 after the infusion ended. This increase was almost completely abolished  
 by pretreatment with desipramine. Apparently, the increased plasma  
 norepinephrine levels seen in some patients with essential hypertension  
 result from increased sympathetic neural activity and not from decreased  
 clearance of norepinephrine, changes in the isoproterenol/norepinephrine  
 ratio after simultaneous infusion of both provide an index of neuronal  
 norepinephrine uptake in man, and neuronal norepinephrine uptake is not  
 stereospecific.  
 ACCESSION NUMBER: 1984:4252 CAPLUS  
 DOCUMENT NUMBER: 100:4252  
 TITLE: Plasma l-[3H]norepinephrine, d-[14C]norepinephrine,  
 and d,l-[3H]isoproterenol kinetics in essential  
 hypertension  
 AUTHOR(S): Goldstein, David S.; Horwitz, David; Keiser, Harry  
 R.;  
 Polinsky, Ronald J.; Kopin, Irwin J.  
 CORPORATE SOURCE: Natl. Heart, Lung, Blood Inst., Bethesda, MD, 20205,  
 USA  
 SOURCE: Journal of Clinical Investigation (1983), 72(5),  
 1748-58  
 CODEN: JCINAO; ISSN: 0021-9738  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English



L16 ANSWER 31 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Harding-Passey mouse-melanoma tyrosinase (EC 1.14.18.1) is inhibited during L-DOPA oxidation by reaction products. L-3,4-Dihydroxyphenyl[3-14C]alanine oxidation products bind to the enzyme, as demonstrated by gel electrophoresis and radioactivity measurements. The enzyme interacts with indoles and oxidizes dopamine and norepinephrine. L-Epinephrine activates tyrosinase at nonhormonal concns., and bovine serum albumin protects the enzyme from autoinhibition. The inhibition of the Harding-Passey mouse-melanoma tyrosinase, during substrate oxidation, is very similar to that of the mushroom enzyme.

ACCESSION NUMBER: 1983:175466 CAPLUS  
 DOCUMENT NUMBER: 98:175466  
 TITLE: Harding-Passey mouse melanoma tyrosinase inactivation by reaction products and activation by L-epinephrine  
 AUTHOR(S): Miranda, Michele; Botti, Dario  
 CORPORATE SOURCE: Ist. Biol. Gen., Univ. Aquila, L'Aquila, 67100, Italy  
 SOURCE: General Pharmacology (1983), 14(2), 231-7  
 CODEN: GEPHDP; ISSN: 0306-3623  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 32 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB Mean arterial pressure was significantly decreased by nifedipine (I) (21829-25-4) in acute and chronic treatment in hypertensive patients, and the antihypertensive effect was enhanced by metoprolol (37350-58-6),

mean arterial pressure did not change in controls in acute administration, while heart rate in these subjects was slower with added metoprolol. No significant change in heart rate was found with nifedipine, but patients in combined treatment had a lower heart rate. The plasma renin (9015-94-5) activity increase due to nifedipine was inhibited both in acute and in chronic treatment by the addition of metoprolol.

Norepinephrine (51-41-2) showed a significant increase in both acute and chronic treatment with nifedipine, and the same pattern was shown with the combined treatment. Epinephrine (51-43-4) remained unchanged in all cases. The results confirm the effectiveness of nifedipine as an antihypertensive agent. This action was enhanced by metoprolol. The plasma renin activity stimulation due to nifedipine was reduced by metoprolol, while norepinephrine was only slightly affected. Nevertheless the combination of nifedipine with metoprolol seemed to reduce the sympathetic overactivity due to vasodilator alone.

Apparently, antihypertensive therapy with combined drugs (nifedipine and metoprolol) is a safer, more effective, and rational treatment than the vasodilator alone.

ACCESSION NUMBER: 1980:597993 CAPLUS  
 DOCUMENT NUMBER: 93:197993  
 TITLE: Acute and long-term effects of nifedipine on plasma renin activity and plasma catecholamines in controls and hypertensive patients before and after metoprolol  
 AUTHOR(S): Corea, L.; Alunni, G.; Bentivoglio, M.; Boschetti, E.; Cosmi, F.; Giaino, M. D.; Miele, N.; Motolese, M.  
 CORPORATE SOURCE: Ist. Semeiotica Med., Univ. Perugia, Perugia, Italy  
 SOURCE: Acta Therapeutica (1980), 6(2), 177-89  
 CODEN: ACTTDZ; ISSN: 0378-0619  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

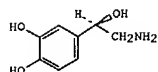
L16 ANSWER 33 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Palytoxin (PTX) (11077-03-3) caused a slow phasic contraction of the isolated guinea-pig vas deferens (2nd component) followed by the 1st rapid phasic contraction (1st component) at  $>3 \times 10^{-9}$ M. N-Acetyl palytoxin (73070-85-6) also produced similar actions but its potency was approx. 1/100 of that of PTX. The 2nd component of PTX-induced contraction, but not the 1st component, was inhibited by treatments with phenolamine methanesulfonate (65-28-1), reserpine (50-55-5), and 6-hydroxydopamine (1199-18-4), but remained unaffected by atropine sulfate (55-48-1) and mecamylamine-HCl (826-39-1) pretreatment. Tetrodotoxin (4368-28-9) partially inhibited the 2nd component, whereas the 2nd component was inhibited by solns. low in Na<sup>+</sup> (85.2 mM) or containing verapamil (52-53-9) (10-6M). Both components were abolished by high Mg or Ca-free medium. Thus, the 1st component was the result of a direct action of PTX on smooth muscle sites, whereas the 2nd phase was the result of an indirect action mediated through the norepinephrine bitartrate (51-40-1) release from the adrenergic nerve terminals.

ACCESSION NUMBER: 1980:526734 CAPLUS  
 DOCUMENT NUMBER: 93:126734  
 TITLE: Mechanism of the excitatory action of palytoxin and N-acetyl palytoxin in the isolated guinea-pig vas deferens  
 AUTHOR(S): Ohizumi, Y.; Shibata, S.  
 CORPORATE SOURCE: Sch. Med., Univ. Hawaii, Honolulu, HI, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1980), 214(1), 209-212  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 34 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The reaction kinetics of norepinephrine N-methyltransferase (I) with m-octopamine-HCl (II) were compared with those for L-norepinephrine bitartrate (III). At high substrate concentration, excess II inhibited I activity. When the concentration of II was varied over a 25-400  $\mu$ M range, however, linear kinetics were obtained with Km and Vmax values of 89  $\mu$ M and 210 nmol/30 min, resp. Comparison of these values with those for III (concentration variation of 5-67  $\mu$ M) indicated that II has a lower affinity for I than does III. Nonetheless, II is methylated at a Vmax similar to that for III and, hence, the methylation of II may occur physiol. or after administration of II in the treatment of hypotension.

ACCESSION NUMBER: 1980:421557 CAPLUS  
 DOCUMENT NUMBER: 93:21557  
 TITLE: m-Octopamine as a substrate for norepinephrine N-methyltransferase  
 AUTHOR(S): Fuller, Ray W.; Hemrick, Susan K.  
 CORPORATE SOURCE: Lilly Res. Lab., Indianapolis, IN, 46285, USA  
 SOURCE: IRCS Medical Science: Library Compendium (1980), 8(5), 284  
 CODEN: IRLCDZ; ISSN: 0305-6651  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 35 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
GI



AB Rabbit aorta microsomes bound 3H-labeled l-norepinephrine (I) [51-41-2] to both high and low affinity sites. Both unlabeled d- and l-norepinephrine isomers equally displaced (20%) of the label from the binding site. The catechol-O-methyltransferase inhibitor inhibited binding by 80%, whereas the monoamine oxidase inhibitor pargyline inhibited binding by only 8.5%. With enzymic sites unrelated to receptor sites blocked by drugs it was determined that the high affinity site was capable of binding 10 pmoles 1/mg microsomal protein and the dissociation constant was  $1.2 \times 10^{-6}$ M. Binding of the  $\alpha$ -antagonist dihydroergocryptine [25447-66-9] to bovine aorta microsomes was rapid and specific. Specific binding was saturable but represented only 21-9% of the total dihydroergocryptine binding to this preparation

ACCESSION NUMBER: 1978:574057 CAPLUS  
DOCUMENT NUMBER: 88:174057  
TITLE: Binding of adrenergic agonist L-(3H)-norepinephrine and antagonist (3H)-dihydroergocryptine to the microsomal fraction of beef and rabbit aorta

AUTHOR(S): Carman-Krzan, Marija  
CORPORATE SOURCE: Med. Fac., Univ. Ljubljana, Ljubljana, Yugoslavia  
SOURCE: Polish Journal of Pharmacology and Pharmacy (1978), 30(2-3), 281-92  
CODEN: PJPPAA; ISSN: 0301-0244

DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 37 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
AB A fluorometric procedure is described for the determination of ng amts. of serotonin, norepinephrine, and dopamine in small brain areas (20-350 mg) from individual rats. The amines were separated from their precursor amino acids and acid metabolites by column chromatog. on Bio-Rex 70 (Na<sup>+</sup>-form, 200-400 mesh). It is possible quant. to determine 10-30 ng of each amine when all 3 are measured simultaneously. When either serotonin or the catecholamines are assayed in a tissue sample, 25-15 ng may be detected. Recoveries of the amines ranged 85-93% as measured by the addition of 14C-labeled amines to tissue supernatants.

ACCESSION NUMBER: 1978:148380 CAPLUS  
DOCUMENT NUMBER: 88:148380  
TITLE: Simultaneous determination of indole- and catecholamines in small brain regions in the rat using a weak cation exchange resin

AUTHOR(S): Holman, R. Bruce; Angwin, Pamela; Barchas, Jack D.  
CORPORATE SOURCE: Dep. Psychiatr. Behav. Sci., Stanford Univ. Sch. Med., Stanford, CA, USA  
SOURCE: Neuroscience (Oxford, United Kingdom) (1976), 1(2), 147-50  
CODEN: NRSCDN; ISSN: 0306-4522

DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 36 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
AB 1,6-Di-O-(2-isocyano-3-methylcrotonyl)-D-mannitol (A32390A) [61241-59-6] is an isonitrile-containing derivative of diacyl D-mannitol. The compound is produced in fermentation as the major component of a metabolic complex known as A32390. A32390A inhibits dopamine- $\beta$ -hydroxylase, reduces heart and adrenal norepinephrine levels, lowers blood pressure in hypertensive rats, and possesses antibiotic activity vs. gram-pos. bacteria and fungi. A32390 is produced in submerged culture by a mold, a species of Pyrenochaeta, NRRL-5786. Glucose and sucrose are among the best C sources for the biosynthesis of A32390. Mannitol, although a substituent of the A32390A mol., supports little or no biosynthesis of the compound when employed as the major C source for the fermentation. The addition of crotonic acid derivs., EtOH, or L-histidine to the fermentation medium enhances the level of A32390 produced.

ACCESSION NUMBER: 1978:168438 CAPLUS  
DOCUMENT NUMBER: 88:168438  
TITLE: A32390A, a new biologically active metabolite. I. Discovery and fermentation studies

AUTHOR(S): Boeck, L. D.; Hoehn, M. M.; Sands, T. H.; Wetzell, R. W.  
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, USA  
SOURCE: Journal of Antibiotics (1978), 31(1), 19-26  
CODEN: JANTAJ; ISSN: 0021-8820

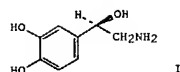
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 38 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
AB In the title method, 50  $\mu$ L blood plasma or tissue extract was incubated with catechol O-methyltransferase and S-adenosylmethionine-3H. The catecholamines were converted to their O-methylated 3H-labeled derivs. These derivs. were purified by solvent extraction and were isolated by 1-dimensional silica gel thin-layer chromatograph. The spots containing the O-methylated derivs. were scraped directly into vials and were determined by liquid scintillation counting. Approx. 1 pg of each catecholamine could be measured with interassay relative standard deviations of 4.3, 8.9, and 13.2% for norepinephrine, epinephrine, and dopamine, resp. No cross-reactivity was noted for several compds. related to these catecholamines.

ACCESSION NUMBER: 1978:47203 CAPLUS  
DOCUMENT NUMBER: 88:47203  
TITLE: A simple specific radioenzymatic assay for the simultaneous measurement of picogram quantities of norepinephrine, epinephrine, and dopamine in plasma and tissues

AUTHOR(S): Sole, Michael J.; Hussain, M. Nasir  
CORPORATE SOURCE: Dep. Med., Univ. Toronto, Toronto, ON, Can.  
SOURCE: Biochemical Medicine (1977), 18(3), 301-7  
CODEN: BIMDA2; ISSN: 0006-2944

DOCUMENT TYPE: Journal  
LANGUAGE: English



AB The effect of intraarterially administered norepinephrine-HCl (I-HCl) [329-56-6] on spinal cord blood flow (SCBF), before and after disruption of the blood-cord barrier was studied in dogs. Barrier disruption was accomplished with an intraarterial bolus injection of 2.5M urea.

Multiple ligations of branches of the posterior aorta and cannula placements ensured that the urea was directed to the lumbar and sacral segments of the cord. Intraarterial urea by itself had no effect on SCBF. The intraarterial infusion of I (12 and 30 µg/min) was without overall effect on SCBF. However, if the blood-cord barrier had been previously disrupted with hypertonic urea, both concns. of I resulted in large decreases in SCBF. No such decreases in SCBF were seen with blood-cord barrier disruption and I if the animals had been pretreated with the α-blocker, phenoxybenzamine (1.5 mg/kg). Some aspects of the possible involvement of I in the pathophysiol. of acute spinal injury are discussed.

ACCESSION NUMBER: 1978:849 CAPLUS  
DOCUMENT NUMBER: 88:849  
TITLE: The effect of norepinephrine on the spinal cord circulation and its possible implications in the pathogenesis of acute spinal trauma  
AUTHOR(S): Crawford, Robert A.; Griffiths, Ian R.; McCulloch, James  
CORPORATE SOURCE: Wellcome Surg. Res. Inst., Glasgow, UK  
SOURCE: Journal of Neurosurgery (1977) 47(4), 567-76  
CODEN: JONSAC; ISSN: 0022-3085  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 41 OF 128 CAPLUS COPYRIGHT 2004 ACS ON STN  
AB In isolated guinea pig hearts perfused with Krebs-Henseleit solution (pH 7.4,

37°), coronary flow, contractile force, coronary sinus O levels, and adenosine [58-61-7] and its degradative products in perfusates were measured before and during the infusion of varying doses of L-epinephrine-HCl [55-31-2], 1-norepinephrine bitartrate [51-40-1], histaminediphosphate [51-74-1], or nitroglycerin [55-63-0]. All 4

compds. produced increases in coronary flow. The catecholamines and histamine had a pos. inotropic effect, increased myocardial O consumption, and decreased coronary sinus O levels. The decrease in coronary sinus O was accompanied by increased levels of adenosine in the perfusates. Nitroglycerin, on the other hand, did not change contractile force, increased coronary sinus O levels, and did not increase the rate of adenosine release. Changes in inosine [58-63-9] and hypoxanthine [68-94-0], degradative products of adenosine metabolism, paralleled those of adenosine in all expts.

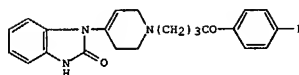
Apparently, adenosine release is intimately associated with a decrease of coronary sinus O levels.  
ACCESSION NUMBER: 1977:512275 CAPLUS  
DOCUMENT NUMBER: 87:112275  
TITLE: Effects of catecholamines, histamine, and nitroglycerin on flow, oxygen utilization, and adenosine production in the perfused guinea pig heart  
AUTHOR(S): Wiedmeier, Vernon, T.; Spell, Larry H.  
CORPORATE SOURCE: Dep. Physiol., Med. Coll. Georgia, Augusta, GA, USA  
SOURCE: Circulation Research (1977), 41(4), 503-8  
CODEN: CIRUAL; ISSN: 0009-7330  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 40 OF 128 CAPLUS COPYRIGHT 2004 ACS ON STN  
AB The GABA [56-12-2] agonist muscimol [2763-96-4] (0.44 nmol), the endogenous opiate receptor β-endorphin [60617-12-1] (1.46 nmol), and norepinephrine [51-41-2] (60 nmol) stimulated food intake in satiated

rats when injected into the ventromedial hypothalamus. Eating induced by muscimol was inhibited by bicuculline, but not by naltrexone or phentolamine, whereas norepinephrine-induced eating was terminated by phentolamine and bicuculline; β-endorphin-induced eating was blocked by both naltrexone and bicuculline. The results implicate GABA in the regulation of food intake and suggest that it may be involved in the increased food intake induced by norepinephrine or opiate receptor agonists.

ACCESSION NUMBER: 1977:594490 CAPLUS  
DOCUMENT NUMBER: 87:194490  
TITLE: Stimulation of food intake by muscimol and beta endorphin  
AUTHOR(S): Grandison, L.; Guidotti, A.  
CORPORATE SOURCE: Lab. Preclin. Pharmacol., St. Elizabeth Hosp., Washington, DC, USA  
SOURCE: Neuropharmacology (1977), 16(7-8), 533-6  
CODEN: NEPHBW; ISSN: 0028-3908  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 42 OF 128 CAPLUS COPYRIGHT 2004 ACS ON STN  
GI



AB The effect of droperidol (I) [548-73-2] on the vasoconstriction induced by norepinephrine, sympathetic nerve stimulation, histamine and K ions was studied on isolated, perfused ear arteries; its effect on norepinephrine-induced contraction was studied on isolated aorta, spleen and vas deferens. In addition, the onset and duration of action of I

was studied. Low doses of I inhibited the vasoconstriction induced by norepinephrine and sympathetic nerve stimulation in the ear artery of rabbit (3.3 + 10<sup>-7</sup> M and 1.3 + 10<sup>-8</sup> M respectively). At similar low doses, I inhibited norepinephrine-induced contractions in the other tissues studied and had a potency comparable to that of phentolamine; its action was rapid in onset and of short duration. High doses of I (10<sup>-6</sup> M) also inhibited the vasoconstriction of the ear artery induced by histamine and by K ions. Thus, at low doses, I has specific and competitive α-adrenoceptor blocking effects.

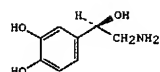
ACCESSION NUMBER: 1977:495623 CAPLUS  
DOCUMENT NUMBER: 87:95623  
TITLE: Specific α-adrenoceptor blocking effect of droperidol on isolated smooth muscles  
AUTHOR(S): Van Nueten, Jan M.; Reneman, Robert S.; Janssen, Paul A. J.  
CORPORATE SOURCE: Dep. Pharmacol., Janssen Pharm., Beerse, Belg.  
SOURCE: European Journal of Pharmacology (1977), 44(1), 1-8  
CODEN: EJPHAZ; ISSN: 0014-2999  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 43 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Pentobarbital (I) [57-33-0] (20-200µM, 180-s exposure) dose-dependently reduced the Ca-dependent efflux of both norepinephrine (II) [51-41-2] and GABA [56-12-2] from K-depolarized mouse forebrain synaptosomal fractions. I did not reduce either II or GABA release in the absence of Ca or the Ca-dependent release facilitated by A23187 [52665-69-7], but Ca-dependent release in the presence of K or veratridine [71-62-5] was depressed by I. The site of action of I in the stimulus-secretion coupling process may be the depolarization-triggered Ca permeation.

ACCESSION NUMBER: 1977:400118 CAPLUS  
 DOCUMENT NUMBER: 87:118  
 TITLE: Pentobarbital depression of stimulus-secretion coupling in brain. Selective inhibition of depolarization-induced calcium-dependent release

AUTHOR(S): Haycock, John W.; Levy, William B.; Cotman, Carl W.  
 CORPORATE SOURCE: Dep. Psychobiol., Univ. California, Irvine, CA, USA  
 SOURCE: Biochemical Pharmacology (1977), 26(2), 159-61  
 CODEN: BCPA6; ISSN: 0006-2952  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 44 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI

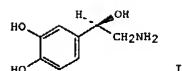


AB Effects of biogenic amines and peptides on urine outflow and antidiuretic hormone (ADH) [11000-17-2] release were studied using rat intracerebroventricular (i.c.v.) perfusion expts. and isolated rat neurohypophysis incubation studies. A decrease in the urine outflow was observed after norepinephrine bitartrate (I) [51-40-1], histamine-2HCl [56-92-8], and 5-valine-angiotensin II amide [53-73-6] were administered i.c.v. The effect of I was prevented by phentolamine mesylate [65-28-1]. Phentolamine alone also acted as an antidiuretic. When the isolated neurohypophysis was incubated in the presence of I, histamine, 5-valine-angiotensin II amide, or bradykinin [58-82-2], release of ADH was increased, and the effects of I and histamine were prevented by phentolamine and promethazine, resp. Phentolamine but not promethazine alone increased ADH release. On the other hand, serotonin, dopamine and 5-isoleucine-angiotensin II did not result in an ADH release from the isolated neural lobes. Apparently, when the local concentration of I, histamine, or peptides is increased to the extent where the posterior lobe of the pituitary is stimulated directly, the ADH release is enhanced.

ACCESSION NUMBER: 1977:183681 CAPLUS  
 DOCUMENT NUMBER: 86:183681  
 TITLE: Antidiuresis of centrally administered amines and peptides and release of antidiuretic hormone from isolated rat neurohypophysis

AUTHOR(S): Hisada, Shiro; Fujimoto, Seigo; Kamiya, Toshio; Endo, Yoshiko; Tsushima, Hiromi  
 CORPORATE SOURCE: Med. Sch., Nagoya City Univ., Nagoya, Japan  
 SOURCE: Japanese Journal of Pharmacology (1977), 27(1), 153-61  
 CODEN: JJPAAZ; ISSN: 0021-5198  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 45 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB The effects of renal nerve stimulation (RNS) and norepinephrine (I) [51-41-2] infusion on the intrarenal distribution of renal blood flow were studied in the isolated blood-perfused canine kidney. Both RNS and I caused a redistribution of fractional blood flow from the inner half to the outer half of the renal cortex. Both vasoconstrictor stimuli resulted in a relatively greater vasoconstriction of the inner cortical vasculature. The inner cortical vasculature is apparently more responsive to vasoactive stimuli and may be the important locus for regulation of the distribution of renal cortical blood flow.

ACCESSION NUMBER: 1977:133908 CAPLUS  
 DOCUMENT NUMBER: 86:133908  
 TITLE: Redistribution of renal cortical blood flow by renal nerve stimulation and norepinephrine infusion

AUTHOR(S): Gotshall, R. W.; Itskovitz, H. D.  
 CORPORATE SOURCE: Sch. Med., Wright State Univ., Dayton, OH, USA  
 SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1977), 154(1), 60-4  
 CODEN: PSEBAA; ISSN: 0037-9727  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 46 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Unavailable

ACCESSION NUMBER: 1977:69199 CAPLUS  
 DOCUMENT NUMBER: 86:69199  
 TITLE: 6-Hydroxydopamine depletion of brain norepinephrine lowers isolation-induced male mouse fighting behavior

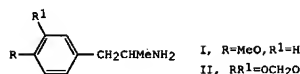
AUTHOR(S): Crawley, Jacqueline N.  
 CORPORATE SOURCE: Univ. Maryland, College Park, MD, USA  
 SOURCE: (1976) 107 pp. Avail.: Xerox Univ. Microfilms, Ann Arbor, Mich., Order No. 76-27,372  
 From: Diss. Abstr. Int. B 1976, 37(6), 2705  
 Dissertation  
 LANGUAGE: English

L16 ANSWER 47 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Norepinephrine, but not dopamine, was increased in both the hypothalamus and telencephalon of genetically obese mice. In the telencephalon norepinephrine turnover time following  $\alpha$ -methyl-p-tyrosine methyl ester administration was slower than that observed in the hypothalamus.

For the obese mice the 95% confidence limits of the regression lines for hypothalamic and telencephalic norepinephrine did not overlap, suggesting a faster turnover time in the hypothalamus than in the telencephalon. This difference was not observed in lean littermates.

ACCESSION NUMBER: 1977:41230 CAPLUS  
 DOCUMENT NUMBER: 86:41230  
 TITLE: Central catechol amine turnover in genetically obese mice (obob)  
 AUTHOR(S): Lorden, Joan F.; Oltmans, Gary A.; Margules, David L.  
 CORPORATE SOURCE: Dep. Psychol., Temple Univ., Philadelphia, PA, USA  
 SOURCE: Brain Research (1976), 117(2), 357-61  
 CODEN: BRREAP; ISSN: 0006-8993  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

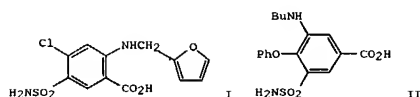
L16 ANSWER 48 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB The ability of various drugs to prevent the lethal effects of 4-methoxyamphetamine-HCl (I-HCl) [3706-26-1] and 3,4-methylenedioxyamphetamine-HCl (II-HCl) [6292-91-7] were reduced by pretreatment with phentolamine mesylate [65-28-1] and 6-hydroxydopamine-HBr [636-00-0] suggesting that release of norepinephrine from peripheral adrenergic nerves contributed to their toxicity. Pretreatment with methysergide bimalate [129-49-7] reduced the lethal effects of (+)-[51-63-8] and (-)-amphetamine sulfate [51-62-7], I, II, and 2,5-dimethoxy-4-methylamphetamine [15588-95-1] suggesting that an action on serotonergic receptors contributed to their toxicity. Pretreatment with 4-chloro-amphetamine, practolol and haloperidol did not alter the lethal effects of the agents studied.

ACCESSION NUMBER: 1976:516772 CAPLUS  
 DOCUMENT NUMBER: 85:116772  
 TITLE: The protective effects of methysergide, 6-hydroxydopamine and other agents on the toxicity of amphetamine, phentermine, MDA, FMA, and STP in mice  
 AUTHOR(S): Lopatka, J. E.; Brewerton, C. N.; Brooks, D. S.; Cook, D. A.; Paton, D. M.  
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Alberta, Edmonton, AB, Can.  
 SOURCE: Research Communications in Chemical Pathology and Pharmacology (1976), 14(4), 677-87  
 CODEN: RCOCB8; ISSN: 0034-5164  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 49 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB Furosemide (I) [54-31-9] (10 or 40  $\mu$ g/ml), bumetanide (II) [28395-03-1] (1 or 4  $\mu$ g/ml), and indomethacin [53-86-1] (5  $\mu$ g/ml) inhibited the pressor response of the rat mesenteric vascular bed to norepinephrine [51-41-2]; in each case responsiveness was restored by prostaglandin E<sub>2</sub> [363-24-6]. I and II failed to inhibit responsiveness in the presence of an adequate amount (50  $\mu$ g/ml) of prostaglandin E<sub>2</sub>. Ovine prolactin [9002-62-4] at a concentration of 50 ng/ml enhanced pressor responses to norepinephrine, but at 500 ng/ml inhibited responsiveness after an initial potentiation. Aspirin [50-78-2] (10 mg/ml), I, and II all reversed both potentiation produced by the lower prolactin concentration and the inhibition produced by the higher one. In light of previous findings, these results suggest that the diuretics exert their vascular effects by inhibiting prostaglandin synthesis, whereas prolactin acts by stimulating such synthesis.

ACCESSION NUMBER: 1976:472106 CAPLUS  
 DOCUMENT NUMBER: 85:72106  
 TITLE: Vascular actions of furosemide and bumetanide on the rat superior mesenteric vascular bed: interactions with prolactin and prostaglandins  
 AUTHOR(S): Mtabaji, J. P.; Manku, M. S.; Horrobin, D. F.  
 CORPORATE SOURCE: Dep. Physiol., Univ. Newcastle upon Tyne, Newcastle upon Tyne, UK  
 SOURCE: Canadian Journal of Physiology and Pharmacology (1976), 54(3), 357-66  
 CODEN: CJPFA3; ISSN: 0008-4212  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 50 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A marked, reversible decline in cardiac norepinephrine stores was noted after exptl. myocardial infarction. Uptake and accumulation of tracer doses of DL-norepinephrine-7-<sup>14</sup>C, as well as the rate of degradation, appeared to be unchanged. Despite marked variation in pool size, the subcellular distribution appeared to be unchanged, and no preferential uptake into any subcellular fraction was observed.

ACCESSION NUMBER: 1976:403555 CAPLUS  
 DOCUMENT NUMBER: 85:3555  
 TITLE: Metabolism of norepinephrine in noninfarcted heart muscle after experimental myocardial infarction  
 AUTHOR(S): Mathes, P.; Sack, D. W.; Gudbjarnason, S.  
 CORPORATE SOURCE: I. Med. Klin., Tech. Univ. Muenchen, Munich, Fed. Rep. Ger.  
 SOURCE: Recent Advances in Studies on Cardiac Structure and Metabolism (1976), 7(Biochem. Pharmacol. Myocardial Hypertrophy, Hypoxia, Infarction), 283-7  
 CODEN: RCSMCP; ISSN: 0363-5872  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 51 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Selective stimulation of the carotid body receptors in dogs by hypoxic, hypercapnic, acidotic blood (venous blood perfusion) produced bradycardia, an increase of coronary flow, and greater release of norepinephrine from the heart; the coronary resistances were decreased. The same stimulation after vagotomy was no longer accompanied by bradycardia. Under these conditions, the decrease of coronary resistance was less marked, and the release of norepinephrine was increased.

ACCESSION NUMBER: 1976:403326 CAPLUS  
 DOCUMENT NUMBER: 85:3326  
 TITLE: Carotid body control of coronary flow, myocardial oxidative metabolism, and cardiac catechol amines in the dog

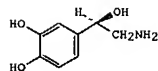
AUTHOR(S): Limet, R.; Chabi, E.; Welch, K. M. A.; Kennedy, J. H.  
 CORPORATE SOURCE: Cora and Webb Mading Dep. Surg., Baylor Coll. Med., Houston, TX, USA  
 SOURCE: Recent Advances in Studies on Cardiac Structure and Metabolism (1976), 9(Sarcolemma), 269-78  
 CODEN: RSCMCP; ISSN: 0363-5872  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 52 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB In normally cycling women studied daily from day 10 to 17 of the menstrual cycle, the levels of circulating norepinephrine (I) showed a sharp rise preceding or concomitant with the ovulatory LH surge. In 2 of 3 patients the I peak took place 24 h before the LH rise; in the 3rd patient the I peak occurred simultaneously. The simultaneous determination of ovarian hormones and I showed no temporal correlation between I and either estradiol or progesterone. On the other hand, after a single i.v. 100 µg dose of LH-releasing hormone (LH-RH), a significant rise in plasma I, preceding the LH peak, was found in the patients studied. The determination of I at 3 min intervals beginning 1 min after LH-RH injection showed a significant rise in the I levels ranging 5-10 times higher than the basal values between 1 and 6 mins after LH-RH stimulation. In these patients a 2nd peak of I occurred simultaneously with the maximum response of LH, which rose to peak levels after 18 min in 1 patient and after 24 min in another. These findings are discussed with respect to the origin and role of increased amts. of plasma I related to the LH surge.

ACCESSION NUMBER: 1976:162530 CAPLUS  
 DOCUMENT NUMBER: 84:162530  
 TITLE: Plasma levels of norepinephrine (NE) during the periovulatory period and after LH-RH stimulation in women

AUTHOR(S): Rosner, Jorge M.; Nagle, C. A.; De Laborde, N. P.; Pedroza, E.; Badano, A.; Figueroa Casas, P. R.; Carril, M.  
 CORPORATE SOURCE: Inst. Latinoam. Fisiol. Reprod., Univ. Salvador, San Miguel, Argent.  
 SOURCE: American Journal of Obstetrics and Gynecology (1976), 124(6), 567-72  
 CODEN: AJOGAH; ISSN: 0002-9378  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 53 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 GI



AB In the absence of exogenously added neurotransmitters sympathetic denervation exerted little effect on the incorporation of 32P into the phospholipids of the excised rabbit iris muscle. In vivo the iris muscle incorporated 32P into phosphatidylinositol, phosphatidic acid, phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine and sphingomyelin in that order of activity while in vitro phosphatidylinositol was followed by phosphatidylcholine. Tension responses of iris dilator muscle from dehydrated irises exhibited supersensitivity to norepinephrine (I) [51-41-2]. Furthermore, I at concns. of 3 µM and 30 mM produced 1.6 times and 3 times stimulation of the phosphatidic acid of the denervated muscle resp. In contrast at 30 µM it stimulated this phospholipid by 1.6 times in the normal muscle. This stimulation was completely blocked by phentolamine. Whereas in the normal muscle acetylcholine [51-84-3] stimulated the labeling of phosphatidic acid and phosphatidylinositol by more than 2 times, in the denervated muscle it only stimulated 1.4 to 1.7 times. Similarly when 32P was administered intracamerally, the labeling found in the various phospholipids of the denervated iris was significantly lower than that of the normal. Apparently, denervation decreases the 32P labeling in the presence of acetylcholine. The I-stimulated 32P incorporation into phosphatidic acid appears to be post-synaptic.

ACCESSION NUMBER: 1976:145150 CAPLUS  
 DOCUMENT NUMBER: 84:145150  
 TITLE: Effects of norepinephrine and acetylcholine on phosphorous-32 incorporation into phospholipids of the rabbit iris muscle following unilateral superior cervical ganglionectomy

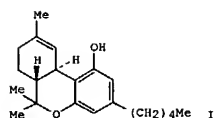
AUTHOR(S): Abdel-Latif, Ata A.; Green, Keith; Matheny, James L.; McPherson, James C., Jr.; Smith, Jack P.  
 CORPORATE SOURCE: Dep. Cell Mol. Biol., Med. Coll. Georgia, Augusta, GA, USA  
 SOURCE: Life Sciences (1975), 17(12), 1821-8  
 CODEN: LIFSAK; ISSN: 0024-3205  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 54 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Isolated brown fat cells from hamster responded to added catechol amines with a temporary increase in respiratory rate and an extended lipolysis. From expts. with catechol amines and α and β-blockers, the receptors of these cells are classified as β according to classical definition. Norepinephrine [51-41-2] induced a rapid increase in cyclic-AMP [60-92-4] levels which paralleled in time the stimulated respiration. Maximum cyclic AMP levels were reached within 1-3 min and were followed by a continuous decline. Parallel to the catechol amine-induced respiration and lipolysis there was a pronounced drop in ATP [56-63-5] levels. This energy depletion was reversed by addition of the β-blocker propranolol within 5 min after norepinephrine. The nucleotide pattern in isolated hamster brown fat cells after norepinephrine addition was mimicked in expts. with isolated hamster brown fat mitochondria. A high ratio of AMP and ADP over ATP decreases the respiratory rate when endogenous free fatty acids are oxidized.

ACCESSION NUMBER: 1976:130560 CAPLUS  
 DOCUMENT NUMBER: 84:130560  
 TITLE: Norepinephrine-induced shift in levels of adenosine 3',5'-monophosphate and ATP parallel to increased respiratory rate and lipolysis in isolated hamster brown-fat cells

AUTHOR(S): Pettersson, Bertil; Vallin, Ivar  
 CORPORATE SOURCE: Wenner-Gren Inst., Univ. Stockholm, Stockholm, Swed.  
 SOURCE: European Journal of Biochemistry (1976), 62(2), 383-90  
 CODEN: EJBCAI; ISSN: 0014-2956  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 55 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
GI



AB Cardiovascular effects of Δ<sup>8</sup>- [5957-75-5] and Δ<sup>9</sup>- tetrahydrocannabinol (I) [1972-08-3] were studied after systemic i.v. administration and intra-arterial (i.a.) administration into a perfused vascular bed in the urethane-anesthetized rat. I.v. administration of the drugs produced dose-related transient increases in blood pressure followed by more prolonged hypotensive responses and bradycardia. Intra-arterial administration into the perfused hindquarters of the rat produced an increase in perfusion pressure indicative of vasoconstriction. The vasoconstrictor response to the cannabinoids corresponded temporally to a similar response produced by i.a. norepinephrine bitartrate [51-40-1] and was in contrast in the more prolonged vasoconstrictor responses produced by vasopressin [11000-17-2]. Phentolamine, in a dose which reduced the vasoconstrictor effect of norepinephrine by 90%, significantly reduced the response to i.a. I while having no effect on the actions of i.a. vasopressin. Reserpine pretreatment significantly reduced vasoconstrictor actions of i.a. tyramine-HCl [60-19-5] and I but did not alter the responses to norepinephrine. These data suggest that the cannabinoids have peripheral vasoconstrictor activity in the rat which may be mediated, in part, through a tyramine-like action on adrenergic nerve terminals.

ACCESSION NUMBER: 1976:130421 CAPLUS  
DOCUMENT NUMBER: 84:130421  
TITLE: Vasoconstrictor actions of Δ<sup>8</sup>- and Δ<sup>9</sup>-tetrahydrocannabinol in the rat  
AUTHOR(S): Adams, M. D.; Earnhardt, J. T.; Dewey, W. L.; Harris, L. S.  
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, USA  
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1976), 196(3), 649-56  
CODEN: JPETAB; ISSN: 0022-3565  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 57 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Sinoaortic denervation (SAD) in the rabbit produced neurogenic hypertension which at 1st was characterized by increased cardiac output and later by increased peripheral vascular resistance. Tyrosine hydroxylase activity and catechol amine concentration of proximal mesenteric artery were greater than those of distal mesenteric vessels in normal rabbits. An hr after SAD norepinephrine (NE) synthesis, the activity of tyrosine hydroxylase assayed in vitro, was increased in proximal mesenteric artery and decreased in distal mesenteric vessels. Eleven and 30 days after SAD, NE synthesis in vivo and the activity of tyrosine hydroxylase assayed in vitro was increased in distal mesenteric vessels and decreased in proximal mesenteric artery. Sympathoadrenal regulation of increased splanchnic vascular resistance was an important factor in initiation and maintenance of neurogenic hypertension in the rabbit.

ACCESSION NUMBER: 1976:28917 CAPLUS  
DOCUMENT NUMBER: 84:28917  
TITLE: Altered norepinephrine synthesis of splanchnic vessels  
AUTHOR(S): in neurogenic hypertension  
CORPORATE SOURCE: Dequattro, Vincent; Alexander, Natalie  
Sch. Med., Univ. South. California, Los Angeles, CA, USA  
SOURCE: European Journal of Pharmacology (1974), 26(2), 231-5  
CODEN: EJPHAZ; ISSN: 0014-2999  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 56 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
GI For diagram(s), see printed CA Issue.

AB The lipolytic effect of norepinephrine (I) [51-41-2] in adipose tissue in vitro was studied before and after exercise in nonfasted rats with severe, untreated streptozotocin diabetes. I in increasing concns. stimulated glycerol release to an equal extent from the adipose tissue of nondiabetic and diabetic rats. However, the reesterification of free fatty acids (FFA) in adipose tissue was decreased by I in diabetic rats as compared to normal rats. During exercise, I further decreased the reesterification of FFA in adipose tissue of diabetic rats. Exercise did not change I-induced glycerol release in the adipose tissue of diabetic rats. In diabetic animals the increase in plasma glycerol and FFA during exercise was correlated inversely with the I-induced release of glycerol and FFA from the adipose tissue of the same animals after exercise. The lipolytic effect of I is not different in adipose tissue of diabetic and nondiabetic rats. By decreasing the reesterification of FFA, I is probably responsible for the observed increase in the release of FFA in vivo, a likely energy source in severely diabetic animals.

ACCESSION NUMBER: 1976:39060 CAPLUS  
DOCUMENT NUMBER: 84:39060  
TITLE: Influence of norepinephrine and exercise on lipolysis in adipose tissue of diabetic rats  
AUTHOR(S): Koivisto, V. A.; Nikkila, E. A.; Akerblom, H. K.  
CORPORATE SOURCE: Child. Hosp., Univ. Helsinki, Helsinki, Finland  
SOURCE: Diabetologia (1975), 11(5), 401-5  
CODEN: DBTGJW; ISSN: 0012-186X  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 58 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

GI For diagram(s), see printed CA Issue.  
AB The effects of 33 phenethylamines and phenethanolamines on uptake of norepinephrine [51-41-2] into cardiac tissue in vivo and release of norepinephrine from cardiac storage sites were determined. The presence of m- or p-hydroxy substituents confers high inhibitory activity, while the o-hydroxy substituted compds. have little or no activity. Inhibitory and release activities were associated with the same general structural features. M-tyramine (I) [588-05-6] and m-octopamine (II) [536-21-0] were nearly equipotent, and among the most active inhibitors of norepinephrine uptake, while neither 6-hydroxynorepinephrine [2623-77-0] nor 6-hydroxyepinephrine [2623-79-2] were active. Structure-activity relations and binding mechanisms are discussed.

ACCESSION NUMBER: 1975:558496 CAPLUS  
DOCUMENT NUMBER: 83:158496  
TITLE: Norepinephrine uptake sites in cardiac tissue. Lack of affinity of 6-hydroxynorepinephrine and related compounds  
AUTHOR(S): Rotman, A.; Lundstrom, J.; McNeal, E.; Daly, J.; Creveling, C. R.  
CORPORATE SOURCE: Natl. Inst. Arthritis, Metab. Dig. Dis., Natl. Inst. Health, Bethesda, MD, USA  
SOURCE: Journal of Medicinal Chemistry (1975), 18(2), 138-42  
CODEN: JMCMAR; ISSN: 0022-2623  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 59 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
GI For diagram(s), see printed CA Issue.

AB The effect of norepinephrine (1) [51-41-2] on the intracellular H<sup>+</sup> concentration of isolated rat hearts perfused with a modified Krebs-Henseleit solution (KHS) was determined. The [H<sup>+</sup>]i was calculated with the [14C]-dimethylxazolidinedione method. Respiratory or metabolic acidosis was produced by equilibrating the KHS and 20% CO<sub>2</sub> or decreasing the [HCO<sub>3</sub><sup>-</sup>] of the KHS, resp. Three types of expts. were carried out: (1) beta blockade-MJ 1999 (Sotalol) was added to the KHS, (2) control-no pharmacol. treatment, and (3) I was added to the KHS. The effective CO<sub>2</sub> buffer values ([HCO<sub>3</sub><sup>-</sup>]i/[A<sub>PI</sub>]) during respiratory acidosis were: beta blockade 11, control 35, and I 84. The production of metabolic acidosis resulted in the following [H<sup>+</sup>]i changes: beta blockade 52 nM, control 60 nM, and I 7 nM. Apparently, I markedly attenuates the change in [H<sup>+</sup>]i accompanying respiratory and metabolic acidosis and may account in part for previous observations that the effective CO<sub>2</sub> buffer value of cardiac muscle in vivo is greater than that in vitro.

ACCESSION NUMBER: 1975:526627 CAPLUS  
DOCUMENT NUMBER: 83:126627  
TITLE: Effect of norepinephrine on myocardial intracellular hydrogen ion concentration  
AUTHOR(S): Riegle, K. M.; Clancy, R. L.  
CORPORATE SOURCE: Med. Cent., Univ. Kansas, Kansas City, KS, USA  
SOURCE: American Journal of Physiology (1975), 229(2), 344-9  
CODEN: AJPHAP; ISSN: 0002-9513  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 60 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
AB Daily oral administration of Pb [7439-92-1] to newborn rats had no adverse

effect on their body growth. Lead-treated rats were more active than age-matched controls. Endogenous levels of brain dopamine [51-61-6] were unchanged, whereas norepinephrine [51-41-2] was increased, suggesting a possible relationship between lead exposure during earliest developmental periods, increased motor activity, and brain norepinephrine, and not brain dopamine as previously postulated.

ACCESSION NUMBER: 1975:401644 CAPLUS  
DOCUMENT NUMBER: 83:1644  
TITLE: Growth, behavior, and brain catechol amines in lead-exposed neonatal rats. Reappraisal  
AUTHOR(S): Golter, Marianne; Michaelson, I. Arthur  
CORPORATE SOURCE: Coll. Med., Univ. Cincinnati, Cincinnati, OH, USA  
SOURCE: Science (Washington, DC, United States) (1975), 187(4174), 359-61  
CODEN: SCIEAS; ISSN: 0036-8075  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 61 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB A procedure for measuring pg quantities of norepinephrine was developed that used partially-purified bovine adrenal phenylethanolamine-N-methyltransferase and 3H-labeled S-adenosylmethionine. The sensitivity of the assay was 25 pg, and the procedure was applicable to many body tissues and fluids, including brain and blood plasma.

ACCESSION NUMBER: 1975:121212 CAPLUS  
DOCUMENT NUMBER: 82:121212  
TITLE: Sensitive radioenzymic assay for norepinephrine in tissues and plasma  
AUTHOR(S): Henry, David P.; Starman, Barbara J.; Johnson, David G.; Williams, Robert H.  
CORPORATE SOURCE: Sch. Med., Univ. Washington, Seattle, WA, USA  
SOURCE: Life Sciences (1975), 16(3), 375-84  
CODEN: LIFSAS; ISSN: 0024-3205  
DOCUMENT TYPE: Journal  
LANGUAGE: English

L16 ANSWER 62 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Male subjects (19-23 years old) underwent a 7-day control period with respect to diet, temperature (22°), and sleep (7.5 hr), followed by a 2-day exposure to 15° and a 2-day recovery period (22°). Urine was collected every 8 hr commencing at 2300 hr and assayed for MHPG and VMA using gas-liquid chromatog. During the control period a diurnal rhythmicity was demonstrated for MHPG and VMA with maxima at 0700-1500 hr.

The mean excretory rates for MHPG and VMA were 0.71 and 2.6 µg/mg creatinine, resp. Cold exposure abolished the rhythms for MHPG and VMA and caused an 18% increase in MHPG excretion. In contrast, VMA excretion was not altered. Significant correlations were obtained with MHPG excretion and both urinary cortisol and rectal temperature. MHPG excretion may be indicative of changes in norepinephrine metabolism in the central nervous system, although alterations in peripheral degradative pathways cannot be ruled out.

ACCESSION NUMBER: 1975:109619 CAPLUS  
DOCUMENT NUMBER: 82:109619  
TITLE: Alteration of circadian rhythmicities of urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) and vanilmandelic acid (VMA) in man during cold exposure  
AUTHOR(S): Cymerman, Allen; Francesconi, Ralph F.  
CORPORATE SOURCE: Mil. Stress Lab., U. S. Army Res. Inst. Environ. Med., Natick, MA, USA  
SOURCE: Life Sciences (1975), 16(2), 225-36  
CODEN: LIFSAS; ISSN: 0024-3205  
DOCUMENT TYPE: Journal  
LANGUAGE: English



L16 ANSWER 63 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Unavailable

ACCESSION NUMBER: 1975:96057 CAPLUS

DOCUMENT NUMBER: 82:96057

TITLE: Inhibition of sacral parasympathetic preganglionic neurons by GABA, glycine, 5-hydroxytryptamine, and norepinephrine

AUTHOR(S): Thomson, Thomas D.

CORPORATE SOURCE: Univ. Utah, Salt Lake City, UT, USA

SOURCE: (1974) 82 pp. Avail.: Xerox Univ. Microfilms, Ann Arbor, Mich., Order No. 74-25,998

From: Diss. Abstr. Int. B 1974, 35(6), 2931

DOCUMENT TYPE: Dissertation

LANGUAGE: English

L16 ANSWER 65 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Long-term regulation of the cyclic AMP phosphodiesterase (9036-21-9) of the C-6 rat glioma cell line has been studied. Both the low Km and high Km activities were induced by elevation of intracellular cyclic AMP [60-92-4] levels following either dibutyryl cyclic AMP [362-74-3] or norepinephrine [51-41-2] treatment of the cells. The presence of either cycloheximide or actinomycin D prevented induction by either dibutyryl cyclic AMP or norepinephrine. Evidence was presented that the norepinephrine effect is mediated by the  $\beta$ -catecholamine receptor. The increased phosphodiesterase activity caused a partial refractoriness to a second challenge with norepinephrine, which could be overcome by blockade of the induction with cycloheximide. Apparently, just as short-term regulation of cyclic AMP levels occurs via changes in the

rates of synthesis or degradation, long-term alterations of the system may also involve either the adenylate cyclase or the phosphodiesterase.

ACCESSION NUMBER: 1975:68555 CAPLUS

DOCUMENT NUMBER: 82:68555

TITLE: Cyclic AMP-mediated induction of the cyclic AMP phosphodiesterase of C-6 glioma cells

AUTHOR(S): Schwartz, Joan P.; Passonneau, Janet V.

CORPORATE SOURCE: Natl. Inst. Neurol. Dis. Stroke, Natl. Inst. Health, Bethesda, MD, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1974), 71(10), 3844-8

CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

L16 ANSWER 64 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Uptake of norepinephrine-3H by slices of the hypothalamus and medial lower brainstem of rats exhibited a significant rhythm with respect to the circadian stage at which the rats were killed. In both regions, the

daily min. uptake was about the same and the time of daily maximum was also

about the same. The maximum uptake occurred in slices prepared 1 hr after the

start of the dark phase. However, the amplitude of the circadian increase in uptake was greater and the circadian decrease in uptake occurred more slowly in the hypothalamus than in the brainstem. The rises above the daily min. were 25 and 20% in the former and the latter regions, resp. The min. in norepinephrine-3H uptake occurred 2 hr after the start of the light phase for the hypothalamus, whereas in the brainstem it occurred at the middle of the dark phase. Thus, 21 components of the uptake or accumulation of norepinephrine show circadian rhythm, and circadian changes in norepinephrine synthesis are probably not sufficient to explain the rhythm in brain region norepinephrine content.

ACCESSION NUMBER: 1975:70991 CAPLUS

DOCUMENT NUMBER: 82:70991

TITLE: Twenty-four-hour rhythmic uptake of tritium-labeled norepinephrine in vitro by hypothalamus and medial lower brainstem

AUTHOR(S): Lew, G. M.; Quay, W. B.

CORPORATE SOURCE: Dep. Zool., Univ. California, Berkeley, CA, USA

SOURCE: International Journal of Chronobiology (1974), 2(2), 209-13

CODEN: IJCBAB; ISSN: 0300-9998

DOCUMENT TYPE: Journal

LANGUAGE: English

L16 ANSWER 66 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB The regulatory influence of thyroid hormone on norepinephrine(I) and its synthesizing enzyme, tyrosine hydroxylase(II), was investigated in developing rat brain. The appearance of brain II was preceded by that of I, since II had attained 75% of adult values 7 days after birth, when the concentration of I was only .apprx.40%. Exptl. cretinism, induced by a

single i.p. injection of 200  $\mu$ Ci of  $^{131}$ I on the day of birth, led to an impairment of the normal developmental increases in the activity of II

and brain I. Whereas 50  $\mu$ Ci of  $^{131}$ I exerted only little effect, 200  $\mu$ Ci inhibited the ontogenic increases in II activity by 31% and in I by 34%. When the radiothyroidectomy was delayed for 20 days, smaller decreases were observed in brain I and II. Treatment of neonatally

thyroidectomized rats with L-triiodothyronine early in life restored the neurochem.

changes in I metabolism in both a time- and dose-dependent manner. When the initiation of L-triiodothyronine treatment was delayed until adulthood, this hormone failed to produce any appreciable change in brain I and II. A critical period apparently exists in early postnatal life during which thyroid hormone is essential for the normal development of brain I

metabolism. The depressed behavior of hypothyroid rats may be related to reduced levels of I at the postsynaptic regions.

ACCESSION NUMBER: 1975:41129 CAPLUS

DOCUMENT NUMBER: 82:41129

TITLE: Alterations in brain norepinephrine and tyrosine hydroxylase activity during experimental hypothyroidism in rats

AUTHOR(S): Rastogi, Ram B.; Singhal, Radhey L.

CORPORATE SOURCE: Dep. Pharmacol., Univ. Ottawa, Ottawa, ON, Can.

SOURCE: Brain Research (1974), 81(2), 253-66

CODEN: BRREAP; ISSN: 0006-8993

DOCUMENT TYPE: Journal

LANGUAGE: English

L16 ANSWER 67 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Noradrenaline regulated thermogenesis during cold adaptation in rats via an effect on  $\beta$ -adrenergic receptors.  
 ACCESSION NUMBER: 1974:533876 CAPLUS  
 DOCUMENT NUMBER: 81:133876  
 TITLE: Noradrenaline and adaptation to cold  
 AUTHOR(S): Pastukhov, Yu. F.  
 CORPORATE SOURCE: Inst. Biol. Probl. Severa, Magadan, USSR  
 SOURCE: Sb. Mater. Nauch. Konf. Fiziol., Biokhim. Farmakol. Zapad.-Sib. Ob'edin., 5th (1973), Meeting Date 1972, 140-1. Editor(s): Larin, E. F. Tomsk. Gos. Univ.: Tomsk, USSR  
 CODEN: 28LYAB  
 DOCUMENT TYPE: Conference  
 LANGUAGE: Russian

L16 ANSWER 68 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB With the possible exception of a slight enhancement of release, neither acute nor chronic administration of synthetic thyrotropin releasing hormone (TRH) [24305-27-9] (8 mg/kg, i.p.) had any effect on the disposition and metabolism of 3H-labeled norepinephrine [51-41-2] in rat brain. In addition, no significant changes were found in brain levels of endogenous norepinephrine, serotonin [50-67-9], or dopamine [51-61-6] following the injection of TRH. Thus, little evidence was found to support a possible relation between the reported clin. antidepressant activity of TRH and its effects on norepinephrine metabolism in the brain.  
 ACCESSION NUMBER: 1974:486363 CAPLUS  
 DOCUMENT NUMBER: 81:86363  
 TITLE: Norepinephrine metabolism in the rat brain following acute and chronic administration of thyrotropin releasing hormone  
 AUTHOR(S): Reigle, Thomas G.; Avni, Jacob; Platz, Patricia A.; Schildkraut, Joseph J.; Plotnikoff, Nicholas P.  
 CORPORATE SOURCE: Dep. Psychiatry, Harvard Med. Sch., Boston, MA, USA  
 SOURCE: Psychopharmacologia (1974), 37(1), 1-6  
 CODEN: PSYPAG; ISSN: 0033-3158  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 69 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Nictitating membrane contractile responses to i.v. infused 1-norepinephrine bitartrate (1) [51-40-1] were increased by denervation (removal of nodose and superior cervical ganglia) or decentralization (removal of a piece of the cervical trunk and vagus). Dose-response data indicated that differences in the degree of decentralization or denervation supersensitivity obtained with I in previous in vivo and in vitro expts. are dependent on whether steady-state or nonsteady-state responses are measured.  
 ACCESSION NUMBER: 1974:433734 CAPLUS  
 DOCUMENT NUMBER: 81:33734  
 TITLE: Sensitivity of the nictitating membrane of the pithed cat to infusions of 1-norepinephrine after denervation or decentralization  
 AUTHOR(S): Tsai, T. H.; Kuhn, W. L.  
 CORPORATE SOURCE: Merrell-Natl. Lab. Div., Richardson-Merrell, Inc., Cincinnati, OH, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1974), 188(3), 630-9  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 70 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A study was done on K uptake and spontaneous rate of discharge in Purkinje fibers from canine hearts perfused in a tissue bath in close proximity to a  $\beta$ -probe. Norepinephrine-induced K uptake was unaffected by lack of O or glucose but was blocked when the energy supply to the Na-K pump or the activity of the pump itself was interfered with by 2-deoxy-D-glucose, low temperature, lack of Mg, strophanthidin, lack of Na, or tetrodotoxin. Norepinephrine apparently increases K uptake by stimulating active transport. In addition, the stimulatory action of norepinephrine on K uptake can be dissociation from its stimulatory action on Purkinje fiber automaticity.  
 ACCESSION NUMBER: 1974:423701 CAPLUS  
 DOCUMENT NUMBER: 81:23701  
 TITLE: Effects of norepinephrine on active potassium ion transport and automaticity in cardiac Purkinje fibers  
 AUTHOR(S): Borasio, P. G.; Vassalle, Mario  
 CORPORATE SOURCE: Dep. Physiol., State Univ. New York, Brooklyn, NY, USA  
 SOURCE: Recent Advances in Studies on Cardiac Structure and Metabolism (1974), 4, 41-57  
 CODEN: RCSMCP; ISSN: 0363-5872  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 71 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The  $\beta_2$  blocking agent N-isopropylmethoxamine (I) [550-53-8] (10-8-10-4 M) significantly antagonized the depressant activity of isoproterenol [7683-59-2], epinephrine [51-43-4], and norepinephrine [51-41-2] on the motility of isolated rabbit detrusor muscle strips, while the  $\beta_1$  blocker, practolol [6673-35-4] (10-8-10-4 M), tended to augment the depressive effects. The data suggested the  $\beta$  receptors of the rabbit detrusor resembled more closely the  $\beta_2$  type than the  $\beta_1$  type.

ACCESSION NUMBER: 1974:409752 CAPLUS  
 DOCUMENT NUMBER: 81:9752  
 TITLE: Selective beta blockade of isolated rabbit detrusor muscle with practolol (AY 21011) and N-isopropylmethoxamine

AUTHOR(S): Anderson, G. F.; Kreulen, D. L.; Fredericks, C. M.  
 CORPORATE SOURCE: Sch. Med., Wayne State Univ., Detroit, MI, USA  
 SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1973), 205(2), 373-80  
 CODEN: AIPTAK; ISSN: 0003-9780  
 JOURNAL

DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 72 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The pressor effect of 2-amino-5-(3,4-dichlorophenoxy)methyl-2-oxazoline (I) [51230-28-5] in dogs was less than that of d-amphetamine sulfate [51-63-8]. Upon repeated administration, tachyphylaxis developed to its pressor but not to its depressor effect. The pressor effect of I was antagonized by pretreatment with reserpine phosphate [1263-94-1] or with phenoxybenzamine-HCl [63-92-3]. I appears to act indirectly through the release of norepinephrine [51-41-2] from peripheral nerve endings. Spinal cordotomy did not significantly affect its pressor activity suggesting that the brain is not involved in its pressor effect. I had a biphasic action on blood pressure: a depressor activity followed by a pressor activity.

ACCESSION NUMBER: 1974:409726 CAPLUS  
 DOCUMENT NUMBER: 81:9726  
 TITLE: Cardiovascular activity of 2-amino-5-(3,4-dichlorophenoxy)methyl-2-oxazoline (APMO)

AUTHOR(S): Abdallah, A. H.; White, H. D.  
 CORPORATE SOURCE: Chem. Biol. Res., Dow Chem. Co., Midland, MI, USA  
 SOURCE: Toxicology and Applied Pharmacology (1973), 26(4), 513-22  
 CODEN: TXAPAS; ISSN: 0041-008X  
 JOURNAL

DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 73 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Incubation of isolated rat epididymal fat cells with 0.2 or 10 nM insulin [9004-10-8] decreased the level of cyclic AMP (I) [60-92-4] in the presence or absence of various lipolytic agents except in the presence of high concns. of catechol amines (0.1-1 mM). When the cells were incubated with 0.01-100 nM insulin, it gave: (a) a biphasic inhibitory effect that was maximal between 0.1 and 1 nM and submaximal at either higher or lower insulin concns on lipolysis stimulated by 0.5 mM dibutyryl I, 10 nM ACTH [9002-60-2], or 1-10  $\mu$ M norepinephrine [51-41-2]; (b) a monophasic inhibitory effect that was maximal at 1-100 nM on lipolysis induced by 5-20 mM I or 1-4 mM caffeine; and (c) a monophasic stimulatory effect that was maximal at 10-100 nM on lipolysis induced by 1 mM dibutyryl I or 0.1-1 mM norepinephrine. Since the insulin inhibitory and stimulatory lipolytic effects seem to be mediated by the cellular insulin receptor or receptors, and not necessarily by decreased I levels, it appears that the insulin receptor system of fat cells can respond to a wide concentration range of the hormone.

ACCESSION NUMBER: 1974:141243 CAPLUS  
 DOCUMENT NUMBER: 80:141243  
 TITLE: Effects of insulin on the levels of adenosine 3',5'-monophosphate and lipolysis in isolated rat epididymal fat cells

AUTHOR(S): Kono, Tetsuro; Barham, Frances, W.  
 CORPORATE SOURCE: Sch. Med., Vanderbilt Univ., Nashville, TN, USA  
 SOURCE: Journal of Biological Chemistry (1973), 248(21), 7417-26  
 CODEN: JBCHA3; ISSN: 0021-9258  
 JOURNAL

DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 74 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB In doca-salt hypertensive rats and spontaneously hypertensive rats the norepinephrine (I) turnover of peripheral and central adrenergic neurons was determined by measuring the rate of decline of endogenous I after inhibition of tyrosine hydroxylase or by measuring the decay of the specific activity after labeling the stores by i.v. or intraventricular injection of [3H]-I. In the 2 types of hypertensive rats turnover in the periphery was delayed in proportion to the rise in systolic blood pressure, whereas in brain stem and residual parts of the brain the I turnover did not differ from that of normotensive controls. In doca-salt hypertension the cardiac I turnover was enhanced in proportion to the rise in blood pressure and reciprocally delayed in brain-stem (medulla-pons, hypothalamus) but not residual parts of the brain. Administration of chlorisondamine, a ganglion-blocking agent which does not cross the blood-brain barrier, resulted in a normalization of both blood pressure and cardiac I turnover, whereas the changes in brain persisted. Encapsulation of the kidney and implantation of doca alone produced neither a rise in blood pressure nor changes in I turnover. It is concluded that in this form of exptl. hypertension the changes in I turnover in the brain stem is causally related to the increased activity of the peripheral sympathetic nervous system which normally is depressed by the activity of the adrenergic neurons in the brain stem. In spontaneously hypertensive rats neither the peripheral nor the central adrenergic nervous system seems to play a primary role in the development of hypertension. The delay in the peripheral I turnover, which is the biochem. correlate of a decreased sympathetic activity, may represent an attempt to compensate for an increased peripheral resistance resulting from changes in the reactivity of vascular smooth muscles or changes in vascular geometry.

ACCESSION NUMBER: 1974:13412 CAPLUS  
 DOCUMENT NUMBER: 80:13412  
 TITLE: Doca [deoxycorticosterone acetate]-salt and spontaneously hypertensive rats. Comparative studies on norepinephrine turnover in central and peripheral adrenergic neurons

AUTHOR(S): Nakamura, Keiji; Gerold, Marcel; Thoenen, Hans  
 CORPORATE SOURCE: Lab. Exp. Med., F. Hoffmann-La Roche Und Co., Basel, Switz.  
 SOURCE: Spontaneous Hypertension (1972), 51-8. Editor(s): Okamoto, Kozo. Igaku Shoin Ltd.: Tokyo, Japan.  
 CODEN: STGTAW  
 CONFERENCE

DOCUMENT TYPE: Conference  
 LANGUAGE: English

L16 ANSWER 75 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Brain norepinephrine metabolism and catechol amine synthesis were measured in rats subjected to elec. footshock in the presence or absence of another subject. Animals shocked in pairs engaged in fighting behavior, whereas animals receiving shock without another rat present could not fight. Marked differences in the metabolism of norepinephrine formed from intracisternally injected dopamine 3-H were found in the 2 groups receiving footshock. Within each exptl. group, alterations in norepinephrine metabolism showed anatomic specificity, and temporal effects on metabolism in various brain regions were observed at various intervals following presentation of footshock. The observed changes in norepinephrine metabolism suggest that in rats receiving footshock without a partner, catechol amine turnover in the medulla-pons specifically increases during the shock period. In contrast, rats shocked in pairs, thereby eliciting fighting responses, show no alterations in regional norepinephrine metabolism during the period of shock.

ACCESSION NUMBER: 1974:1864 CAPLUS  
 DOCUMENT NUMBER: 80:1864  
 TITLE: Brain norepinephrine metabolism and shock-induced fighting behavior in rats. Differential effects of shock and fighting on the neurochemical response to a common footshock stimulus

AUTHOR(S): Stolk, Jon M.; Conner, Robert L.; Levine, Seymour; Barchas, Jack D.  
 CORPORATE SOURCE: Dep. Psychiatry, Stanford Univ., Stanford, CA, USA  
 SOURCE: U. S. Nat. Tech. Inform. Serv., AD Rep. (1973), No. 764072, 60 pp. Avail.: NTIS  
 FROM: Govt. Rep. Announce. (U.S.) 1973, 73(18), 30  
 CODEN: XADRCH  
 DOCUMENT TYPE: Report  
 LANGUAGE: English

L16 ANSWER 76 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Intraventricularly administered dopamine [51-61-6] (200-800 µg) and apomorphine [58-00-4] (10-80 µg) decreased the rearing response in rats but caused a dose-dependent increase in ambulation. Intraventricular norepinephrine [51-41-2] (2-64 µg) and clonidine [4205-90-7] (2-64 µg) decreased both ambulation and rearing. Thus, dopaminergic, but not noradrenergic receptors in the brain appear to be involved in stereotyped behavior.

ACCESSION NUMBER: 1973:532917 CAPLUS  
 DOCUMENT NUMBER: 79:132917  
 TITLE: Effect of substances acting on the central adrenergic receptor on open field behavior in rats

AUTHOR(S): Dandiya, P. C.; Patni, S. K.  
 CORPORATE SOURCE: Dep. Pharmacol., S.M.S. Med. Coll., Jaipur, India  
 SOURCE: Indian Journal of Medical Research (1913-1988) (1973), 61(6), 891-5  
 CODEN: IJMRAQ; ISSN: 0019-5340  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 77 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB In the vagotomized dog, the sinus acceleration induced by perfusion of the sinus node artery with 1µg of dopamine [51-61-6] or 0.1µg of norepinephrine [51-41-2] was suppressed by 30-100µg of haloperidol (I) [52-86-8]. I showed no differentiation of blocking activity between dopamine- and norepinephrine-induced positive chronotropic effects. Injection of more than 100 µg of I frequently caused sinus arrhythmia.

ACCESSION NUMBER: 1973:511750 CAPLUS  
 DOCUMENT NUMBER: 79:111750  
 TITLE: Effect of haloperidol on sinus acceleration responses to dopamine and norepinephrine

AUTHOR(S): Chiba, Shigetoshi; Satoh, Keisuke; Hashimoto, Koroku  
 CORPORATE SOURCE: Sch. Med., Tohoku Univ., Sendai, Japan  
 SOURCE: Tohoku Journal of Experimental Medicine (1973), 110(2), 207-8  
 CODEN: TJEMAO; ISSN: 0040-8727  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 78 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Alpha-blockade virtually abolished the pulmonary pressor responses to hypoxia, hypercapnic acidosis, histamine, and norepinephrine, but did not produce reversal of the pressor response (i.e. vasodilation) to these agents. Reversal of the pulmonary pressor response to epinephrine occurred after alpha-blockade, but the vasodilation was slight and consistent with previous observations of meager vasodilations with isoproterenol without blockade. It is suggested that beta-adrenergic mechanisms are not only relatively scarce in the pulmonary circulation but also are not directly stimulated by hypoxia, hypercapnic acidosis, or histamine. Enhanced pulmonary pressor responses to hypoxia, hypercapnia, and histamine occurred during beta-blockade and may be due to the unmasking of addnl., but previously antagonized, alpha-receptors. Since no significant effect on the pressor response to serotonin was evident from either alpha- or beta-blockade, a different mechanism mediating the pressor response to this agent is suggested.

ACCESSION NUMBER: 1973:430033 CAPLUS  
 DOCUMENT NUMBER: 79:30033  
 TITLE: Adrenergic receptors in pulmonary vasoconstrictor responses to gaseous and humoral agents

AUTHOR(S): Porcelli, Robert J.; Bergofsky, Edward H.  
 CORPORATE SOURCE: Sch. Med., New York Univ., New York, NY, USA  
 SOURCE: Journal of Applied Physiology (1948-1976) (1973), 34(4), 483-8  
 CODEN: JAPYAA; ISSN: 0021-8987  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 79 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB In pithed rats, the potentiation of the pressor response to exogenous or endogenous norepinephrine [51-41-2] by the catechol-o-methyltransferase (COMT) inhibitor, pyrogallol [87-66-1], was enhanced by desipramine-HCl [58-28-6]. In the presence of desipramine, pyrogallol also increased the uptake of norepinephrine-3H by the heart. Thus, the participation of COMT in norepinephrine inactivation must be greater when norepinephrine uptake is inhibited by a potent catechol amine uptake inhibitor, such as desipramine.

ACCESSION NUMBER: 1973:427374 CAPLUS  
 DOCUMENT NUMBER: 79:27374  
 TITLE: Modification by desipramine of the pyrogallol adrenergic sensitization in the rat  
 AUTHOR(S): Caillard, C.; Rapin, J. R.; Bralet, J.; Rossignol, P.  
 CORPORATE SOURCE: Lab. Pharmacodyn., U.E.R. Sci. Pharm. Biol., Paris, Fr.  
 SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1973), 202(1), 153-62  
 CODEN: AIPTAK; ISSN: 0003-9780  
 DOCUMENT TYPE: Journal  
 LANGUAGE: French

L16 ANSWER 80 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Acetylcholine chloride [60-31-1] (5 .tim. 10-8-5 .tim. 10-7 g/ml depressed the contractions and diminished the efflux of tritiated norepinephrine [51-41-2] induced by elec. stimulation of canine saphenous vein strips in vitro. Thus, acetylcholine relaxes venous smooth muscle during sympathetic stimulation by inhibiting the release of norepinephrine from the nerve endings.

ACCESSION NUMBER: 1973:413435 CAPLUS  
 DOCUMENT NUMBER: 79:13435  
 TITLE: Inhibition of tritium labeled norepinephrine release from sympathetic nerve endings in veins by acetylcholine  
 AUTHOR(S): Vanhoutte, Paul M.; Lorenz, Robert R.; Tyce, Gertrude M.  
 CORPORATE SOURCE: Mayo Clin. and Mayo Found., Rochester, MN, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1973), 185(2), 386-94  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 81 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A daily rhythm in norepinephrine (I) content was demonstrated in the brain-stem, diencephalon, and cerebral cortex of hamsters (Mesocricetus auratus), exposed to a 12/12-hr light-dark cycle for a month or longer and then sacrificed at intervals over a 24-hr period. The rhythms in brain-stem and cerebral cortex were reproducible, with the peak in I content in each area occurring during the late light phase. The I rhythm in the brain-stem was demonstrated when different methods for I extraction were utilized.

ACCESSION NUMBER: 1973:157337 CAPLUS  
 DOCUMENT NUMBER: 78:157337  
 TITLE: Daily rhythm in norepinephrine content in regions of the hamster brain  
 AUTHOR(S): Morgan, William M.; McFadin, Linda S.; Harvey, Catherine Y.  
 CORPORATE SOURCE: Med. Sch., Univ. Texas, San Antonio, TX, USA  
 SOURCE: Comparative and General Pharmacology (1973), 4(13), 43-8  
 CODEN: CPGPAY; ISSN: 0010-4035  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 82 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Application of indomethacin, a drug known to inhibit prostaglandin synthesis, to isolated perfused rabbit hearts decreased the release of prostaglandins normally induced by nerve stimulation and simultaneously increased the release of norepinephrine in response to nerve stimulation. Indomethacin itself did not affect norepinephrine release from the heart in the absence of nerve stimulation nor did it affect the uptake of exogenous norepinephrine, suggesting that the increased norepinephrine release reflects disinhibition of a feedback mechanism, using endogenously formed prostaglandins for limitation of norepinephrine release.

ACCESSION NUMBER: 1973:41031 CAPLUS  
 DOCUMENT NUMBER: 78:41031  
 TITLE: Augmented noradrenaline release following nerve stimulation after inhibition of prostaglandin synthesis with indomethacin  
 AUTHOR(S): Junstad, Marianne; Pham Huu Chanh; Wennmalm, Ake  
 CORPORATE SOURCE: Dep. Physiol., Karolinska Inst., Stockholm, Swed.  
 SOURCE: Acta Physiologica Scandinavica (1972), 86(4), 563-7  
 CODEN: APSCAX; ISSN: 0001-6772  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 83 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB In anesthetized cats, endogenous norepinephrine [51-41-2], epinephrine [51-43-4], and dopamine [51-61-6] released from the adrenal medulla and sympathetic nerve endings inhibited transmission in the stellate ganglion.  
 The actions of these catechol amines were inhibited by adrenergic  $\alpha$ -receptor blockade. Isoproterenol [7683-59-2] increased the ganglionic transmission but this action was inhibited by  $\beta$ -receptor blockade. The preganglionic nerve stimulation in the stellate ganglion produced an increase in left intraventricular pressure but this response was depressed by topical application of norepinephrine to the stellate ganglion.

ACCESSION NUMBER: 1973:24372 CAPLUS  
 DOCUMENT NUMBER: 78:24372  
 TITLE: Effects of catechol amines on sympathetic evoked action potentials in the stellate ganglion of the cat  
 AUTHOR(S): Sakanashi, Matao  
 CORPORATE SOURCE: Med. Sch., Kumamoto Univ., Kumamoto, Japan  
 SOURCE: Japanese Journal of Pharmacology (1972), 22(3), 391-401  
 CODEN: JJPAAZ; ISSN: 0021-5198  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 84 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A new method was developed for the determination of amines and amine turnover in tissues using gas chromatog. followed by mass spectral fragmentation of the effluent products. The method was applied to catechol amines in rat ganglia. Reserpine (I) [50-55-5] (0.1 and 0.5 mg/kg) depleted norepinephrine [51-41-2] by 82 and 92%, resp. In contrast, the dopamine [51-61-6] levels were unchanged and decreased 53%, resp.

ACCESSION NUMBER: 1973:256 CAPLUS  
 DOCUMENT NUMBER: 78:256  
 TITLE: Gas chromatography-mass fragmentography. New approach  
 AUTHOR(S): to the estimation of amines and amine turnover  
 CORPORATE SOURCE: Cattabeni, F.; Koslow, S. H.; Costa, E.  
 SOURCE: Saint Elizabeths Hosp., Washington, DC, USA  
 Advances in Biochemical Psychopharmacology (1972), 6, 37-59  
 CODEN: ABPYBL; ISSN: 0065-2229  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 85 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A special proteolipid extracted from bovine spleen capsules with CHCl<sub>3</sub>-MeOH (2:1), separated by column chromatog. on Sephadex LH-20, and eluted between 17 and 22 ml CHCl<sub>3</sub> bound 3H-labeled (+)-norepinephrine [138-65-8]. The saturation curve of the binding indicated that the proteolipid contained 2 groups of sites with different dissociation consts. For 200,000 g proteolipid, 3 moles of norepinephrine were bound with high affinity and 27 moles with low affinity. Binding of norepinephrine to the receptor proteolipid was competitively inhibited by the  $\alpha$ -adrenergic blocking agents, phentolamine [50-60-2] and dibenamine [51-50-3], and by the  $\beta$ -adrenergic blocking agent, propranolol [525-66-6].

ACCESSION NUMBER: 1972:429507 CAPLUS  
 DOCUMENT NUMBER: 77:29507  
 TITLE: Isolation of a proteolipid from spleen capsule binding  
 AUTHOR(S): (+)-[3H]-norepinephrine  
 CORPORATE SOURCE: Fiszler de Plazas, Sara; De Robertis, Eduardo  
 SOURCE: Fac. Med., Univ. Buenos Aires, Buenos Aires, Argent.  
 Biochimica et Biophysica Acta (1972), 266(1), 246-54  
 CODEN: BBACAQ; ISSN: 0006-3002  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 86 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Halothane [151-67-7], cyclopropane [75-19-4], Ethrane [13838-16-9], and diethyl ether [60-29-7] added in concns. producing a 50% decrease in the myocardial isometric contractile force of isolated guinea pig left atria did not affect either the uptake of 3H-labeled 1-norepinephrine [51-41-2] or the intraneuronal monoamine oxidase [9001-66-5] activity.

ACCESSION NUMBER: 1972:413979 CAPLUS  
 DOCUMENT NUMBER: 77:13979  
 TITLE: Effects of inhalation anesthetics on the uptake and metabolism of 1-3H-norepinephrine in guinea-pig atria  
 AUTHOR(S): Brown, Burnell R., Jr.; Tatum, Ella N.; Crout, J. Richard  
 CORPORATE SOURCE: Southwest. Med. Sch., Univ. Texas, Dallas, TX, USA  
 SOURCE: Anesthesiology (1972), 36(3), 263-7  
 CODEN: ANESAV; ISSN: 0003-3022  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 87 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Aggression caused by prolonged isolation of rats was accompanied by an increased content of free and a decreased content of bound norepinephrine [51-41-2] in the brain. A sedative dose of the neuroleptic, haloperidol (I) [52-86-8], (2 mg/kg) decreased the content of both free and bound fractions of norepinephrine in the brain. In animals with expl. aggressiveness, I decreased the level of the free functionally active fraction of norepinephrine, but did not affect the bound fraction. Seduxen (diazepam) (II) [439-14-5], a tranquilizer, in the same dose decreased the content of the free fraction of norepinephrine in the brain stem of control and isolated rats.

ACCESSION NUMBER: 1972:135724 CAPLUS  
 DOCUMENT NUMBER: 76:135724  
 TITLE: Influence of neuroleptics and tranquilizers on the levels of free and bound norepinephrine fractions in the brain of rats during aggression

AUTHOR(S): Vysotskaya, N. B.; Boiko, S. S.; Aleashinkova, T. N.  
 CORPORATE SOURCE: Inst. Pharmacol., Moscow, USSR  
 SOURCE: Byulleten Eksperimental'noi Biologii i Meditsiny (1972), 73(1), 58-60  
 CODEN: BEBMJE; ISSN: 0365-9615

DOCUMENT TYPE: Journal  
 LANGUAGE: Russian

L16 ANSWER 88 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Norepinephrine-3H (I) was infused intraarterially at a constant rate of 1, 5, or 50 ng/min into the cat spleen, perfused with Krebs-bicarbonate solution. In the course of I infusion, splenic nerves were stimulated at frequencies of 5 and 30 sec-1 for 1 min, the total norepinephrine (II), and I of the perfusate collected during stimulation, were measured; nerves were also stimulated after infusion of I. During infusion at different rates, 55% of the infused radioactivity was recovered in the venous perfusate. Of the radioactivity so recovered, approx.70% was due to II. Perfusing the spleen at varying flow rates (2-13 ml/min) did not appreciably affect recoveries. During stimulation at a frequency of 30 sec-1, there was a net increase in I output over the background level. In spleens perfused with either low Ca or high Mg Krebs solution, the increase in I outflow in response to nerve stimulation during I infusion was considerably reduced, but the sp. activity of the released amine was not appreciably altered. Sp. activities of II released by nerve stimulation during infusion of I were comparable, or only slightly higher than those obtained after stopping the infusion of the amine. Retention of I during its infusion was also not significantly different in stimulated and nonstimulated portions of the same spleen. It is concluded that increase in I outflow during stimulation is probably due to enhanced release, and that nerve stimulation does not appreciably affect the uptake of infused I.

ACCESSION NUMBER: 1972:111147 CAPLUS  
 DOCUMENT NUMBER: 76:111147  
 TITLE: Effects of nerve stimulation on the uptake of norepinephrine by the perfused spleen of the cat

AUTHOR(S): Yamamoto, H.; Kirpekar, S. M.  
 CORPORATE SOURCE: Downstate Med. Cent., State Univ. New York, Brooklyn, NY, USA  
 SOURCE: European Journal of Pharmacology (1972), 17(1), 25-33  
 CODEN: EJPHAZ; ISSN: 0014-2999

DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 89 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Isolated rat irides from untreated rats or rats pretreated with the tyrosine hydroxylase inhibitor H44/68 or the dopamine- $\beta$ -hydroxylase inhibitor FLA63 were incubated in physiol. buffer for 30 min and then superfused by buffer for 60 min in small chambers. Some of the irides were stimulated by an elec. field at 10 Hz for 60 min. Endogenous noradrenaline (NA) was enzymically determined or the irides were examined with the fluorescence histochem. method. Irises that were not stimulated contained about 5 ng NA/iris. Stimulation reduced the NA content of irides from untreated or FLA63 pretreated rats to approx.60% of the unstimulated control. Stimulation caused an altered distribution of NA with a less pronounced cumulation of NA to the varicosities of the adrenergic nerve terminals. Addition of tyrosine to the superfusing buffer did not diminish the stimulation-induced decrease of NA. In irides from rats pretreated with H44/68, stimulation reduced the NA content to approx.25% of the unstimulated control. A great reduction of the fluorescence intensity of the majority of the nerve terminals was observed. The difference found in stimulation-induced depletion of endogenous NA between irides of untreated and H44/68 pretreated rats is most likely due to synthesis of NA in vitro in the irides of untreated rats.

ACCESSION NUMBER: 1972:110966 CAPLUS  
 DOCUMENT NUMBER: 76:110966  
 TITLE: Synthesis of noradrenaline in isolated rat iris during field stimulation

AUTHOR(S): Farnebo, Lars O.; Lidbrink, Peter  
 CORPORATE SOURCE: Dep. Histol., Karolinska Inst., Stockholm, Swed.  
 SOURCE: Acta Physiologica Scandinavica, Supplementum (1971), No. 371, 29-34  
 CODEN: APSSAD; ISSN: 0302-2994

DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 90 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Bioassays for epinephrine (I) and norepinephrine(II) were done on adrenal glands from goats, sheep, cats, and rats at various stages of pregnancy and postpartum. Also, 24-hr urinary output of I and II were determined in 20 women in pregnancy, in labor, and postpartally. Results indicate that none of these 3 states produces significant changes in the I and II content of the adrenal glands. Urinary I and II output remains normal until the onset of labor when there is a marked increase in both, especially II. Postpartally there is a gradual rise in I and II, peaking at 6-18 hr after delivery. A case of hydatidiform mole (Deastrusens) showed normal I and II urinary output. Small amts. of both were found in the mole.

ACCESSION NUMBER: 1972:83905 CAPLUS  
 DOCUMENT NUMBER: 76:83905  
 TITLE: Epinephrine and norepinephrine in pregnancy. Comparative study of the adrenal gland and catechol output in different species of animals and man

AUTHOR(S): Goodall, McC.; Diddle, A. W.  
 CORPORATE SOURCE: Med. Branch, Univ. Texas, Galveston, TX, USA  
 SOURCE: American Journal of Obstetrics and Gynecology (1971), 111(7), 896-904  
 CODEN: AJOGAH; ISSN: 0002-9378

DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 91 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Nialamide (I) [51-12-7] pretreatment of isolated arteries produced a secondary increase in the constrictor response to extraluminal norepinephrine [51-41-2], as well as a delayed recovery from the effects of norepinephrine. Chronically denervated arteries did not display the secondary response or delayed recovery, suggesting that these actions were associated with inhibition of intraneuronal rather than extraneuronal monoamine oxidase. I treatment did not influence the effect of intraluminal norepinephrine, apparently due to the relative failure of intraluminal norepinephrine to penetrate to the sympathetic nerve terminals.

ACCESSION NUMBER: 1972:81454 CAPLUS  
 DOCUMENT NUMBER: 76:81454  
 TITLE: Relation between the roles of monoamine oxidase and sympathetic nerves in the vasoconstrictor response of the rabbit ear artery to norepinephrine  
 AUTHOR(S): De la Lande, I. S.; Jellet, L. B.  
 CORPORATE SOURCE: Dep. Hum. Physiol. Pharmacol., Univ. Adelaide, Adelaide, Australia  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1972), 180(1), 47-55  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 92 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The brain of dogs were relatively protected from anoxia caused by either decreases in inspired oxygen [7782-44-7] concentration or by sludging in the microcirculation. The administration of norepinephrine (I) [51-41-2] at 2 µg/kg moderately increased the arterial pressure with simultaneous increases in arterial, renal, and cerebral O2 pressure (pO2). Higher doses markedly increased the arterial pressure with a decrease in arterial, renal, and cerebral pO2. Thus attempts to support the circulation with I should strive for low doses with only modest increases in pressure.

ACCESSION NUMBER: 1972:54385 CAPLUS  
 DOCUMENT NUMBER: 76:54385  
 TITLE: Effect of norepinephrine, blood sludging, and respiratory agas change on blood and tissue oxygenation as determined with ultramicro oxygen electrodes  
 AUTHOR(S): Bicher, H. I.; Fitts, C. T.; Yarbrough, D. R., III  
 CORPORATE SOURCE: Dep. Anat., Med. Univ. South Carolina, Charleston, SC, USA  
 SOURCE: Surgical Forum (1971), 22, 213-15  
 CODEN: SUFOAX; ISSN: 0071-8041  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 93 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Norepinephrine (I) [51-41-2] stimulated glucose [50-99-7] uptake in erythrocytes and lymphocytes and inhibited it in the lymphoblast. This action was partially inhibited in the erythrocyte and was converted to inhibition in the lymphocyte by phenolamine [50-60-2]. Thus, I's effect in both is an alpha adrenergic action. The lymphoblast inhibition of glucose uptake by I was converted to stimulation by addition of propranolol [525-66-6] which indicated the I acts in this case through a beta receptor mechanism.

ACCESSION NUMBER: 1972:10464 CAPLUS  
 DOCUMENT NUMBER: 76:10464  
 TITLE: Alpha adrenergic stimulation of glucose uptake in the human erythrocyte, lymphocyte, and lymphoblast  
 AUTHOR(S): Hadden, J. W.; Hadden, Elba M.; Good, R. A.  
 CORPORATE SOURCE: Dep. Pediatr., Variety Club Heart Hosp., Minneapolis, MN, USA  
 SOURCE: Experimental Cell Research (1971), 68(1), 217-19  
 CODEN: ECREAL; ISSN: 0014-4827  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 94 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The effects of different derivs. of tyrosine (I) are considered. Reserpine given alone to rats, gave a 3-fold increase in I transaminase (II). However, rats pretreated with the monoamine oxidase inhibitor Catron showed no depletion of brain norepinephrine (III) and no significant rise in II. Incubation of II with III plus the pyridoxal 5'-phosphate (IV) cofactor inhibited III activity as much as 95%.

Maximum inhibition occurred only on precubation of III with the reaction mixture. There was spectrophotometric evidence (curves shown) of complex formation between III and IV. An isobestic point of 345 mµ indicated that the reaction can be treated in terms of a single equilibrium between IV and the product of its reaction with III. Similar effects of other complexes of amines with IV are considered, in relation to substituents on the amines. Increasing concns. of III reduced and finally abolished the induction of II by pyridoxine. A mechanism is discussed by which III may contribute to the II activity rhythm.

ACCESSION NUMBER: 1971:459335 CAPLUS  
 DOCUMENT NUMBER: 75:59335  
 TITLE: Norepinephrine and the circadian rhythm of rat hepatic tyrosine transaminase activity  
 AUTHOR(S): Black, Ira B.  
 CORPORATE SOURCE: Natl. Inst. Ment. Health, Bethesda, MD, USA  
 SOURCE: Biogenic Amines Physiol. Regul., Symp. (1970), Meeting  
 Date 1969, 301-20. Editor(s): Blum, J. J.  
 Prentice-Hall, Inc.: Englewood Cliffs, N. J.  
 CODEN: 23BPAZ  
 Conference  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English



L16 ANSWER 95 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Rats under anaesthesia were injected with 14C-or 3H-labeled noradrenaline.  
 The animals were killed after 0.5-30 min and samples taken according to Ullberg (1954) for autoradiog. The results showed binding within 1 min in the adrenal medulla and sympathetic adrenergic plexus of innervated tissues and organs. Absorption, probably from the plasma, was also demonstrated within 1 min in extraneuronal tissues, e.g. myocardial fibers. Medullary epinephrine may, by competition, diminish or limit the uptake of norepinephrine into the extraneuronal pool(s).  
 ACCESSION NUMBER: 1971:50202 CAPLUS  
 DOCUMENT NUMBER: 74:50202  
 TITLE: Uptake and storage of carbon-14- and tritium-labeled norepinephrine in rats  
 AUTHOR(S): Leder, O.; Harms, E.; Kammermeier, H.  
 CORPORATE SOURCE: Physiol. Inst., Univ. Freiburg/Br., Freiburg/Br., Fed.  
 SOURCE: Rep. Ger. Histochemie (1970), 24(2), 130-41  
 CODEN: HICHAU; ISSN: 0018-2222  
 DOCUMENT TYPE: Journal  
 LANGUAGE: German

L16 ANSWER 96 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB On incubation with crude mitochondrial fractions from various areas of rabbit brain with 5-hydroxytryptamine (I), the increase in the levels of I in the hypothalamus and corpus striatum was much higher than that in the whole brain stem; the increase in the cerebellum was quite small. Dopamine (II) and norepinephrine (III) reduced the level of I incorporation into the hypothalamus by 20-50%, resp., and II and III reduced incorporation into the corpus striatum by 50%. II did not alter the uptake in the cerebellum and III inhibited it only slightly. There is evidently a considerable degree of regional specificity in the uptake of I by I terminals since the exogenous I was mostly taken up by crude mitochondrial fractions from areas rich in endogenous I.  
 ACCESSION NUMBER: 1970:423025 CAPLUS  
 DOCUMENT NUMBER: 73:23025  
 TITLE: Regional specificity of 5-hydroxytryptamine uptake in rabbit brain stem  
 AUTHOR(S): Takatsuka, K.; Segawa, Tomio; Takagi, Hiroshi  
 CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, Japan  
 SOURCE: Journal of Neurochemistry (1970), 17(5), 695-6  
 CODEN: JONRA9; ISSN: 0022-3042  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 97 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB N-Ethoxycarbonyl-3-morpholinoyldonitamine (I) (0.10-2.0 mg/kg) given i.v. to anesthetized dogs and cats produced a gradually developing and prolonged hypotensive effect characterized by a decrease in pulse pressure because of the greater fall in systolic than diastolic pressure. The hypotension was not antagonized by pretreatment with atropine sulfate (1 mg/kg i.v.), bilateral cervical vagotomy, spinal cord section with cervical vagotomy, or evisceration. During the hypotensive effect, the pressor response to bilateral carotid occlusion and the response of the nictitating membrane to preganglionic sympathetic stimulation were not affected, and blood pressure responses to epinephrine-HCl and norepinephrine-HCl were not consistently affected although I reduced the responses at the perfused vascular bed to the catechol amines but not to angiotensin II given directly into the perfusion circuit. These results suggested that I did not produce its hypotensive effect through central, sympathetic, and parasympathetic nervous systems or a specific blockade of the  $\alpha$ -adrenergic receptive system. The rates of blood flow in the femoral and coronary arteries of dogs were not increased by intraarterial injections of I, and the decreased in parallel with the hypotension induced by i.v. injection of the drug. In constant flow perfusion expts., the perfusion pressure of the femoral artery was not reduced in parallel with I-induced hypotension. These results indicate that I-induced hypotension resulted not from a dilator action of peripheral resistance vessels but rather from a decreased cardiac output by either a decreased venous return or by a depressed cardiac function. The drug did not affect isolated atria, ventricular strip, and ileum in a concentration from 1 to 100  $\mu$ g/ml. I was active orally as sublingually in anesthetized dogs.  
 ACCESSION NUMBER: 1970:402430 CAPLUS  
 DOCUMENT NUMBER: 73:2430  
 TITLE: Hypotensive action of N-ethoxycarbonyl-3-morpholinoyldonitamine, SIN-10  
 AUTHOR(S): Kikuchi, Kenzo; Hirata, Minoru; Nagaoka, Akinobu  
 CORPORATE SOURCE: Biol. Res. Lab., Takeda Chem. Ind., Ltd., Osaka, Japan  
 SOURCE: Japanese Journal of Pharmacology (1970), 20(1), 102-15  
 CODEN: JJPAAZ; ISSN: 0021-5198  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 98 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The effects of L-noradrenaline (1-4  $\mu$ g/kg i.v.), Na pentobarbital (4-6 mg/kg) and adrenolitic (1,6-dimethyl-8 $\beta$ -(5-bromonicotinoyloxymethyl)met hoxerygoline) (50-299  $\mu$ g/kg) on the cerebral blood flow, the cortical pH, pCO<sub>2</sub>, and pO<sub>2</sub>, the end-expiratory CO<sub>2</sub> concentration, and on the arterial pressure were studied in cats. During artificial respiration noradrenaline increased cerebral blood flow, pH, pO<sub>2</sub>, and arterial pressure, reduced pCO<sub>2</sub>, and did not affect end-expiratory CO<sub>2</sub> levels within 1 min; similar results were produced during spontaneous respiration except that pH was decreased and pCO<sub>2</sub> was increased. Within 15 min, pentobarbital decreased cerebral blood flow, pCO<sub>2</sub>, pO<sub>2</sub>, arterial pressure, and end-expiratory CO<sub>2</sub> and increased pH during artificial respiration; during spontaneous respiration, pH was decreased, pCO<sub>2</sub> and end-expiratory CO<sub>2</sub> increased, and the decrease in blood flow was less by a factor of 9 and the pO<sub>2</sub> and arterial pressure were 6 and 2.5 times more than during artificial respiration. One min after the adrenolitic injection in artificially respiring cats, blood flow, pH, pO<sub>2</sub>, and arterial pressure were reduced and pCO<sub>2</sub> was increased; during spontaneous respiration, the decreases in blood flow and pH were greater but the effects on the other parameters were of lesser magnitude than during artificial respiration. Acidification of the cerebral cortex increased cerebral blood flow and reduced cerebral vascular resistance, while alkalization produced the opposite effects. The reactions of cerebral vascular resistance during the action of different vasoactive agents are modified by simultaneous influences on the H<sup>+</sup> concns. in the vascular walls of the resistance vessels. The variation in H<sup>+</sup> concns. are not only caused by local metabolic changes linked to functional cortical changes but also by variations in the transport of substances through vascular walls and by variations in ventilation. Since blood pressure and cortical vascular resistance are interacting with acid-base variations of the cortex, the organism can compensate extreme variations of 1 of these factors by variation of other factors in this meso regulatory system.  
 ACCESSION NUMBER: 1970:129069 CAPLUS  
 DOCUMENT NUMBER: 72:129069  
 TITLE: Regulation of local cortical cerebral blood flow following injections of norepinephrine, pentobarbital, and adrenolitic  
 AUTHOR(S): Blummueller, Heinrich; Betz, Eberhard  
 CORPORATE SOURCE: Physiol. Inst., Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.  
 SOURCE: Aerztliche Forschung (1970), 24(4), 97-111  
 CODEN: ARZFAN; ISSN: 0001-9496  
 DOCUMENT TYPE: Journal  
 LANGUAGE: German

L16 ANSWER 99 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Using a sinus node-interventricular septum perfusion technique, the effects of norepinephrine (5.0 µg/kg, intraarterially), isoproterenol (6.5, or 0.75 µg/kg, intracardially), and sympathetic nerve stimulation upon the myocardium, and the effect of α-adrenergic blockade with verapamil (18 µg/kg, intraarterially, infused for 2-3 min) upon these responses were studied in dogs. Norepinephrine and sympathetic nerve stimulation increased the heart rate of these animals with outbursts of arrhythmias and atrial fibrillation, whereas isoproterenol induced similar increases in the heart rate, but caused no arrhythmias. Pretreatment of dogs with verapamil inhibited both sympathetic nerve stimulation and norepinephrine-induced arrhythmias, enhanced the tachycardia, and increased the contractile force produced by all 3 procedures. The observed responses to sympathetic nerve

stimulation, norepinephrine, and isoproterenol, and their modification by verapamil, may be localized myocardial responses involving both cardiac α- and β-adrenergic mechanisms.

ACCESSION NUMBER: 1970:98857 CAPLUS

DOCUMENT NUMBER: 72:98857

TITLE: Adrenergic mechanisms in the initiation of cardiac arrhythmias

AUTHOR(S): Garvey, H. Lloyd

CORPORATE SOURCE: Fac. Med., Univ. Ottawa, Ottawa, ON, Can.

SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1969), 182(2), 376-90

CODEN: AIPYAK; ISSN: 0003-9780

DOCUMENT TYPE: Journal

LANGUAGE: English

L16 ANSWER 100 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Tyrosine hydroxylase was partially purified from the human pheochromocytoma. Properties of the pheochromocytoma enzyme were similar to those of the bovine adrenal enzyme. The enzyme required tetrahydropteridine as a cofactor and was markedly activated by Fe<sup>2+</sup>. Tyrosine hydroxylase isolated from the human pheochromocytoma was less sensitive to the inhibition by norepinephrine than the enzyme from the bovine adrenal medulla, either in the presence or absence of Fe<sup>2+</sup>. It is suggested that the uncontrolled excessive production of norepinephrine in the pheochromocytoma could be partly due to altered sensitivity of tyrosine hydroxylase to norepinephrine inhibition.

ACCESSION NUMBER: 1970:96844 CAPLUS

DOCUMENT NUMBER: 72:96844

TITLE: Partial separation and properties of tyrosine hydroxylase from the human pheochromocytoma: effect of norepinephrine

AUTHOR(S): Nagatsu, Toshiharu; Yamamoto, Tomiko; Nagatsu, Ikuko

CORPORATE SOURCE: Sch. Dent., Aichi-Gakuin Univ., Nagoya, Japan

SOURCE: Biochimica et Biophysica Acta (1970), 198(2), 210-18

CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

L16 ANSWER 101 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Effects of tyramine (0.5 mg/kg, i.v.), ephedrine (1.0 mg/kg, i.v.), and amphetamine (1.0 mg/kg, i.v.) on arterial blood pressure were studied in dogs with or without pretreatment with nialamide (20 mg/kg, i.p.). The hypertensive effect of tyramine was unaltered by ephedrine and amphetamine, although there was a crossed tachyphylaxis between the α-methylated amines in dogs that were not treated with nialamide. Pretreatment with nialamide increased the pressor effect of tyramine and the crossed tachyphylaxis between tyramine and α-methylated amines. This effect was due to the prolonged occupation of intraneuronal storage sites by tyramine.

ACCESSION NUMBER: 1970:88738 CAPLUS

DOCUMENT NUMBER: 72:88738

TITLE: Crossed tachyphylaxis between tyramine and some alpha methylated sympathomimetic amines

AUTHOR(S): De Moraes, Sergio; Varela de Carvalho, F.; Aragao, J. A.

CORPORATE SOURCE: Fac. Vet Med., Univ. Sao Paulo, Sao Paulo, Brazil

SOURCE: Pharmacology (1970), 3(3), 168-76

CODEN: PHMGBN; ISSN: 0031-7012

DOCUMENT TYPE: Journal

LANGUAGE: English

L16 ANSWER 102 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Catecholaminergic neurons, which take up and retain exogenous norepinephrine-3H, were studied, by means of high-resolution radioautography, in the substantia nigra, the substantia nigra periventricularis, and the locus ceruleus of the rat. Glutaraldehyde was the most suitable fixative for preserving the labeled amine in situ: norepinephrine-3H itself, rather than metabolites, accounted for most of the reactions detected in catecholaminergic neurons. At various time intervals after an intraventricular injection of norepinephrine-3H, the tracer reached a concentration 15-100 times higher, and disappeared at a slower rate, in presynaptic axons (t<sub>1/2</sub> = 4 hr) than in nerve cell bodies (t<sub>1/2</sub> = 0.8-1.3 hr). After pretreatment with a monoamine oxidase inhibitor, the radioautographic reactions increased and persisted longer, especially in the preterminal axons. Within neurons, the labeled amine was ubiquitously distributed in the nerve cell body and concentrated in presynaptic axons and synaptic terminals of various morphol. types. Although large granular vesicles were usually present in the labeled axonal bulbs, no structural characteristic could be specifically ascribed to catecholaminergic neurons. Exogenous norepinephrine bound to macromol. complexes is seemingly present in all parts of catecholaminergic neurons and mainly concd. within presynaptic axons.

ACCESSION NUMBER: 1970:86726 CAPLUS

DOCUMENT NUMBER: 72:86726

TITLE: Intraneural distribution of exogenous norepinephrine in the central nervous system of the rat

AUTHOR(S): Descarries, Laurent; Droz, Bernard

CORPORATE SOURCE: Dep. Biol., C.E.A., Saclay, Fr.

SOURCE: Journal of Cell Biology (1970), 44(2), 385-99

CODEN: JCLBA3; ISSN: 0021-9525

DOCUMENT TYPE: Journal

LANGUAGE: English

L16 ANSWER 103 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The relations between blood flow in epigastric adipose tissue and free fatty acid (FFA) release were studied in rabbits. The close intraarterial infusion of the fat mobilizers, Synacthen,  $\beta$ -MSH, luteotropin, growth hormones, and glucagon, increased blood flow and released FFA into the venous effluent; both fat mobilization and vasodilatation continued for about an hr after termination of infusions. Infusion of norepinephrine, which does not release FFA in rabbit epigastric fat tissue, evoked vasoconstriction. No vasodilator substance was detected in the venous effluent from the activated adipose tissue, but a vasodilator was present in acid-ether exts. of adipose tissue excised during a period of fat mobilization. This suggested that a vasodilator substance is released or formed in adipose tissue during fat mobilization.

ACCESSION NUMBER: 1970:75211 CAPLUS  
 DOCUMENT NUMBER: 72:75211  
 TITLE: Mechanism of functional vasodilatation in rabbit epigastric adipose tissue  
 AUTHOR(S): Lewis, Graham Pritchard; Matthews, John  
 CORPORATE SOURCE: CIBA Lab., Horsham, UK  
 SOURCE: Journal of Physiology (Cambridge, United Kingdom) (1970), 207, 15-30  
 CODEN: JPHYA7; ISSN: 0022-3751  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 104 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Epididymal fat pads of rats treated with lysine vasopressin (100 millimoles/100 g) released significantly less free fatty acids and glycerol than the tissue of control rats. Lysine vasopressin treatment effectively blocked the stimulatory effect of norepinephrine (200  $\mu$ g/100 g s.c.) on adipose tissue lipolysis. Lysine vasopressin (40  $\mu$ U/100 g s.c.), when given in vivo, was a potent inhibitor of hormone-sensitive lipase activity in white adipose tissue. On the other hand, appreciable change was not observed in the lipase activity of brown adipose tissue following lysine vasopressin treatment. Lipoprotein lipase activity of epididymal white fat as well as interscapular brown fat was not affected by either lysine vasopressin or norepinephrine injections.

ACCESSION NUMBER: 1970:51437 CAPLUS  
 DOCUMENT NUMBER: 72:51437  
 TITLE: Inhibition of adipose tissue lipase activity following administration of vasopressin  
 AUTHOR(S): Moriya, Kiyoshi; Itoh, Shinji  
 CORPORATE SOURCE: Sch. Med., Hokkaido Univ., Sapporo, Japan  
 SOURCE: Japanese Journal of Physiology (1969), 19(6), 834-40  
 CODEN: JJPHAM; ISSN: 0021-521X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 105 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Abolition of the circadian rise of plasma 17-hydroxy corticosteroid levels in the cat was produced by types of drugs that alter serotonin levels or action: (1) 3-(2-aminobutyl)indole acetate, which elevates central nervous system serotonin levels; (2) p-chloroamphetamine, which depletes central nervous system serotonin levels; (3) 2'-[[3-(dimethylamino)propyl]thio]cinnamylidide, which acts as a competitive inhibitor of serotonin at the receptor site; and (4) cyproheptadine, which is a serotonin antagonist. L- $\alpha$ -Methyl-p-tyrosine, which lowers central nervous system norepinephrine levels, and reserpine, which lowers both central nervous system serotonin and norepinephrine levels, do not block the circadian rise of plasma 17-hydroxy corticosteroid levels. None of the agents abolishing the circadian rise block: (1) the adrenal response to adrenocorticotrophic hormone; (2) the pituitary-adrenal response to lysine vasopressin; (3) the hypothalamic-pituitary-adrenal response to either insulin hypoglycemia or Pseudomonas polysaccharide administration. Central nervous system mechanisms and (or) structures involved in the regulation of circadian periodicity of adrenal steroid levels are probably different from those mediating stress-initiated adrenal cortical responses.

ACCESSION NUMBER: 1970:40673 CAPLUS  
 DOCUMENT NUMBER: 72:40673  
 TITLE: Serotonin mediation of circadian periodicity of plasma 17-hydroxycorticosteroids  
 AUTHOR(S): Krieger, Dorothy T.; Rizzo, Frank  
 CORPORATE SOURCE: Mt. Sinai Sch. of Med., New York, NY, USA  
 SOURCE: American Journal of Physiology (1969), 217(6), 1703-7  
 CODEN: AJPHAP; ISSN: 0002-9513  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 106 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The uptake of norepinephrine by rabbit platelets at pH 6.0 was increased by Na<sup>+</sup> and to a lesser extent by K<sup>+</sup>. In contrast, the retention of norepinephrine by the platelets was impaired to a greater extent by a lack of K<sup>+</sup> than by a lack of Na<sup>+</sup>. At high levels, K<sup>+</sup> inhibited norepinephrine uptake, whereas Na<sup>+</sup> continued to stimulate norepinephrine uptake over a wide range of concns. The uptake of tryptamine by the platelets was not influenced by changes in the levels of Na<sup>+</sup> and K<sup>+</sup> in the incubation medium. Ouabain inhibited the K<sup>+</sup>- but not the Na<sup>+</sup>-dependent component of norepinephrine uptake. Chlorpromazine and imipramine inhibited both the Na<sup>+</sup> and the K<sup>+</sup>-dependent uptake of norepinephrine, whereas propranolol and phenoxybenzamine inhibited norepinephrine uptake by the inhibition of a process not dependent on either Na<sup>+</sup> or K<sup>+</sup>.

ACCESSION NUMBER: 1969:459320 CAPLUS  
 DOCUMENT NUMBER: 71:59320  
 TITLE: Effects of sodium and potassium on norepinephrine uptake by rabbit platelets and the inhibition of this process by drugs  
 AUTHOR(S): McLean, J. R.; Potoczak, Doris  
 CORPORATE SOURCE: Res. Lab., Parke, Davis and Co., Ann Arbor, MI, USA  
 SOURCE: Archives of Biochemistry and Biophysics (1969), 132(2), 416-22  
 CODEN: ABBIA4; ISSN: 0003-9861  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 107 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Chicks (1-5-days-old) were made hyperactive and aggressive by an injection of 15 mg. imipramine-HCl/kg. Injection of 5-20 micromoles norepinephrine-HCl/kg. 90 min. after treatment with imipramine-HCl produced behavioral depression in the chick in a monotonic, dose-response manner and antagonized the behavioral effects of imipramine-HCl.

Associated with this behavioral antagonism was a relative decrease in the radioactivity in brain normetanephrine and 3-methoxy-4-hydroxymandelic acid when isotopic norepinephrine-HCl was infused following imipramine-HCl pretreatment. Thus, imipramine may block the excess of norepinephrine to the postsynaptic membrane as well as interfering with other aspects of norepinephrine inter- and intracellular mobility.

ACCESSION NUMBER: 1969:429111 CAPLUS  
 DOCUMENT NUMBER: 71:29111  
 TITLE: Imipramine antagonism of the CNS [central nervous system] effects of norepinephrine behavioral and biochemical correlates  
 AUTHOR(S): Mandell, Arnold J.; Spooner, Charles E.; Winters, Wallace D.; Cruikshank, M.; Sabbot, I. M.  
 CORPORATE SOURCE: Brain Res. Inst., Los Angeles, CA, USA  
 SOURCE: International Journal of Neuropharmacology (1969), 8(3), 235-44  
 CODEN: IJNEAQ; ISSN: 0375-9458  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 108 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB There is rapid accumulation of gangliosides (I) with age in mouse, rat, and human brain tissue. This is followed by an accumulation of cerebrosides (II). II and sphingomyelin occur in the myelin sheath; I occurs elsewhere. These lipids are those which provide structural integrity where this integrity must be maintained for a long period of time. A portion of the sphingosine mol. contains a hydroxyl group and an amino group. Its structure is markedly similar to the structure of monoglyceride. Both acetylcholine (III) and I concentrate in the nerve terminal fraction. Subfractionation of the osmotically disrupted nerve terminal fraction into "ghosts" and an enriched synaptic vesicle fraction showed that I is found primarily in the synaptic vesicle fraction which also contains III. The lipids bind III. The vesicle fractions from the brain were relatively nonspecific. They bound III, choline, norepinephrine, serotonin, and  $\gamma$ -aminobutyric acid. This binding, even in the vesicles, was due primarily to the phospholipids, which are spatially oriented and spaced by the cholesterol present. This permits maximum binding of the neurohormones. The nerve terminal fraction binding is probably specific. Active transport may be involved. The binding is not inhibited by K<sup>+</sup> and the bound III is osmotically sensitive.

ACCESSION NUMBER: 1969:1516 CAPLUS  
 DOCUMENT NUMBER: 70:1516  
 TITLE: Lipids and neuronal development  
 AUTHOR(S): Burton, Robert M.  
 CORPORATE SOURCE: Sch. of Med., Washington Univ., St. Louis, MO, USA  
 SOURCE: United States, Public Health Service Publication (1967), No. 1791, 60-75  
 CODEN: XPHFAW; ISSN: 0500-3148  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 109 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB DL- $\alpha$ -Methyltyrosine was injected i.p. into mice in a dose of 80 mg./kg. The mice, which had been previously made aggressive by maintenance in isolation cages, were kept, after treatment, either in isolation, in bisexual pairs, or in groups of 8. Total brain levels of norepinephrine and dopamine were no lower in fighting or grouped mice than in nonstimulated controls, although after 2.5 hrs. the norepinephrine levels were lower in the brain stem and higher in the telencephalon of the fighting mice than in their undisturbed controls. The average dopamine level was slightly higher in stimulated mice in each experiment. Stimulus-induced conservation of brain catechol amines may have compensated for the increased demand for catechol amine release under these conditions. 17 references.

ACCESSION NUMBER: 1968:457836 CAPLUS  
 DOCUMENT NUMBER: 69:57836  
 TITLE: Failure of natural stimuli to accelerate brain catechol amine depletion after biosynthesis inhibition  
 AUTHOR(S): Welch, Annemarie S.; Welch, Bruce L.  
 CORPORATE SOURCE: Mem. Res. Center and Hosp., Knoxville, TN, USA  
 SOURCE: Brain Research (1968), 9(2), 402-5  
 CODEN: BRREAP; ISSN: 0006-8993  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 110 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Metabolic energy of the brain appears to have a crude relationship to consciousness. Exceptions include such conditions as schizophrenia and the psychosis resulting from LSD. During normal sleep O consumption by the brain is not altered, as in coma or anesthesia. Although the mechanism may be obscure, interference with protein synthesis does block the ability to consolidate memory patterns. The disorder of thought processes as in schizophrenia may be the result of an abnormal metabolism of epinephrine into hallucinogenic agents. The mood-altering drugs may act being antagonistic to amines found in the brain. Both these drugs and electroconvulsive shock increased the amount of norepinephrine in the brain of rats.

ACCESSION NUMBER: 1968:434193 CAPLUS  
 DOCUMENT NUMBER: 69:34193  
 TITLE: Biochemistry and mental states  
 AUTHOR(S): Kety, Seymour S.  
 CORPORATE SOURCE: Harvard Med. Sch., Boston, MA, USA  
 SOURCE: California Medicine (1968), 108(5), 362-8  
 CODEN: CAMEAS; ISSN: 0008-1264  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 111 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB In cats, the response of the blood pressure to norepinephrine was enhanced by imipramine, desipramine, atropine, and the antihistaminics, tripeleonnamine, thenyldiamine, carbinoxamine, and chlorpheniramine and was reduced by promazine. The norepinephrine-induced contraction of the nictitating membrane was potentiated significantly by desipramine and to a lesser extent by imipramine, tripeleonnamine, and thenyldiamine, but not by atropine or the other 2 antihistaminics. Hypothermia induced in mice by 2 mg. of reserpine/kg. i.p. was reduced by imipramine, desipramine, amitriptyline, promazine, atropine, and the 4 antihistaminics. Other antihistaminics, including thonzylamine, Antergan, and dimethindene, were inactive. The stimulant effects of dopa in pargyline-pretreated mice was enhanced by the tricyclic antidepressants, atropine, methylatropine, tripeleonnamine, and particularly chlorpheniramine. Chlorpromazine consistently reduced dopa-induced motor hyperactivity. None of the 4 pharmacol. test for non-monoamine oxidase inhibiting antidepressants is specific in that, dependent on the procedure utilized, certain antihistaminics and anticholinergics are active. Only imipramine and desipramine were shown pos. in all 4 procedures.

ACCESSION NUMBER: 1968:417911 CAPLUS  
 DOCUMENT NUMBER: 69:17911  
 TITLE: Effect of imipramine on central adrenergic mechanisms  
 AUTHOR(S): Sigg, E. B.; Hill, R. T.  
 CORPORATE SOURCE: Geigy Res. Div., Geigy Chem. Corp., Ardsley, NY, USA  
 SOURCE: Neuro-Psycho-Pharmacol., Proc. Int. Congr. Coll. Int. Neuro-Psycho-Pharmacol., 5th, Washington, D. C. (1967), Volume Date 1966 367-72  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 113 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Exogenous K<sup>+</sup> potentiated cold (4°) contraction in isolated rat intestine but had no similar effect on guinea pig intestine. Protriptyline, which by itself slightly relaxed the rat vas deferens, greatly potentiated the contractions induced by cold stimulus, K<sup>+</sup>, and norepinephrine. Norepinephrine contraction was not modified by cold stimulation or K<sup>+</sup>. Reserpine was species-specific on the isolated intestine: it abolished cold contraction in guinea pigs, while in rats only the spontaneous movements were decreased. However, the cold response of the intestine in both species was inhibited by in vivo reserpinization. Cooling guinea pig intestine in the presence of reserpine increased K<sup>+</sup> release, a mechanism which may be responsible for some of reserpine's toxic action on contracting organs, such as cardiac insufficiency in rats accompanied by K<sup>+</sup> release and in patients treated with cardiac glycosides and reserpine.

ACCESSION NUMBER: 1968:103659 CAPLUS  
 DOCUMENT NUMBER: 68:103659  
 TITLE: Cold stimulation of organs in relation to potassium concentration and drug action  
 AUTHOR(S): Arbona I., Juan  
 CORPORATE SOURCE: Esc. Med. "Jose Vargas", Univ. Cent. Venezuela, Caracas, Venez.  
 SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1968), 127(2), 359-63  
 CODEN: PSEBAA; ISSN: 0037-9727  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 112 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Tricyclic antidepressants modify the fate of norepinephrine (1) released by reserpine from intraneuronal storage sites in rats in vivo. The change in the metabolic fate of the released 1 is the biochem. basis for the shift in autonomic and behavioral activity which occurs when reserpine-like drugs are administered after tricyclic antidepressants.

ACCESSION NUMBER: 1968:401603 CAPLUS  
 DOCUMENT NUMBER: 69:1603  
 TITLE: Adrenergic mechanisms in the central action of tricyclic antidepressants and substituted phenothiazines  
 AUTHOR(S): Sulzer, F.; Dingell, J. V.  
 CORPORATE SOURCE: Sch. of Med., Vanderbilt Univ., Nashville, TN, USA  
 SOURCE: Aggressologie (1968), 9(2), 281-7  
 CODEN: AGSOA6; ISSN: 0002-1148  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 114 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Addition of caffeine to pig feed, in doses of 1.5 g./kg. of feed during 4 weeks, increased N retention by 7.9% in 65 kg. pigs fed 2 kg. of feed per day. Feeding weanling pigs the same dose of caffeine for several months did not significantly affect feed efficiency, growth rate, and protein content of the carcass, but reduced depth of fat deposition by 6.6-13.1%, as compared with control animals. When given in 3 g./kg. of feed doses, caffeine restricted feed consumption and caused a skin rash. In comparison with control animals, injection of norepinephrine (2 mg./kg., i.m.) into pigs treated with 14C-labeled palmitate increased the level of expired 14C-labeled O<sub>2</sub> up to 10 times and caffeine (50 mg./kg.) treatment increased it up to 6 times, whereas treatment with colchicine (0.1 mg./kg.) had no effect on it. Norepinephrine produced a large increase in the plasma levels of free fatty acids, whereas caffeine produced a moderate increase and colchicine only a slight increase in these levels. Thus, caffeine is capable of mobilizing body fat and, under restricted feeding conditions, of increasing growth rate and feed efficiency in growing pigs. 18 references.

ACCESSION NUMBER: 1968:103064 CAPLUS  
 DOCUMENT NUMBER: 68:103064  
 TITLE: Effect of caffeine on nitrogen retention, carcass composition, fat mobilization, and the oxidation of 14C-labeled body fat in pigs  
 AUTHOR(S): Cunningham, Hugh M.  
 CORPORATE SOURCE: Canada Dep. Agr., Nappan, NS, Can.  
 SOURCE: Journal of Animal Science (Savoy, IL, United States) (1968), 27(2), 424-30  
 CODEN: JANSAG; ISSN: 0021-8812  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 115 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Atria with attached functional sympathetic postganglionic fibers were isolated from rabbits and placed in modified Ringer's solution at 30°. Transmembrane potentials were recorded from pacemaker fibers of the sinoatrial node. Typical effects of sympathetic nerve stimulation were an increase in the slope of slow depolarization during diastole and an acceleration of the pacemaker rate. In .apprx.25% of the pacemaker fibers studied, nerve stimulation did not induce the increase in the slope in spite of marked acceleration of pacemaker rate. The 90% duration was decreased and the depolarization time was prolonged after the stimulation. Similar changes in membrane potentials were induced by the application of norepinephrine. However, the incidence of pacemaker shift was observed more in the presence of norepinephrine than in response to sympathetic stimulation. When the threshold potential was lowered because of the conversion of the true pacemaker fiber to a latent pacemaker fiber, the size of the overshoot was not increased. Similar changes in the action potential duration and the depolarization time in response to sympathetic stimulation and norepinephrine application were elicited when the sinoatrial node was driven at interstimulus intervals of <370 msec. Cardiac norepinephrine might not induce changes in membrane potential during systole but during diastole.

ACCESSION NUMBER: 1967:440600 CAPLUS  
 DOCUMENT NUMBER: 67:40600  
 TITLE: Influence of sympathetic stimulation on transmembrane potentials in the sinoatrial node  
 AUTHOR(S): Toda, Noboru; Shimamoto, Kiro  
 CORPORATE SOURCE: Fac. Med., Kyoto Univ., Kyoto, Japan  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1968), 159(2), 298-305  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 116 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Replacement of 30% of the NaCl content of the modified Krebs-Ringer solution by sucrose to maintain osmolarity had no effect on the frequency of the isolated rabbit auricle but did increase the strength of contraction. Norepinephrine and tyramine showed their normal effects of increasing rate, but did not increase the strength of contraction beyond that due to the low Na content of the medium. Angiotensin did not affect the rate of contraction.

ACCESSION NUMBER: 1967:440600 CAPLUS  
 DOCUMENT NUMBER: 67:40600  
 TITLE: Influence of sodium reduction in the medium on the norepinephrine, tyramine, and angiotensin effects upon the isolated rabbit atria  
 AUTHOR(S): Illanes, Alejandro; Ortiz, Aurelio; Perez-Olea, Jaime  
 CORPORATE SOURCE: Univ. Chile, Santiago, Chile  
 SOURCE: Archivos de Biología y Medicina Experimentales (1966), 3(2-3), 130-5  
 CODEN: ABMXAZ; ISSN: 0004-0533  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Spanish

L16 ANSWER 117 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Rat, rabbit, or bovine phenethanolamine N-methyltransferase, which catalyzes the N-methylation of 1-norepinephrine in the final step of epinephrine biosynthesis, was inhibited in vitro by added epinephrine (100 µM), which sharply reduced velocity without affecting the Km for the substrate. The enzyme might be suppressed in the normal adrenal gland by the presence of high levels of epinephrine. Increased secretion of epinephrine would decrease the amount of product inhibition, resulting in increased methylation of 1-norepinephrine.

ACCESSION NUMBER: 1967:400296 CAPLUS  
 DOCUMENT NUMBER: 67:296  
 TITLE: Inhibition of phenethanolamine N-methyltransferase by its product, epinephrine  
 AUTHOR(S): Fuller, Ray W.; Hunt, Joseph M.  
 CORPORATE SOURCE: Eli Lilly and Co., Indianapolis, IN, USA  
 SOURCE: Life Sciences (1967), 6(10), 1107-12  
 CODEN: LIFSAB; ISSN: 0024-3205  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 118 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Unavailable

ACCESSION NUMBER: 1967:400296 CAPLUS  
 DOCUMENT NUMBER: 67:296  
 TITLE: Studies of the enzymes involved in the biosynthesis of norepinephrine  
 AUTHOR(S): Levitt, Morton  
 CORPORATE SOURCE: Howard Univ., Washington, DC, USA  
 SOURCE: (1967) 147 pp. Avail.: 66-12,471  
 From: Diss. Abstr. B 1967, 27(7), 2462-3  
 DOCUMENT TYPE: Dissertation  
 LANGUAGE: English

L16 ANSWER 119 OF 128 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB cf. preceding abstract The Easson-Stedman hypothesis that dextro isomers of sympathomimetic amines have pharmacol. activities similar to their corresponding deoxy derivs. was tested in the catechol amine-depleted (reserpine, 5 mg./kg., i.p., 16-24 hrs. previously) rat vas deferens. Cumulative dose-response curves were obtained, in vitro, for D- and L-isomers of norepinephrine, epinephrine, cobefrin, metaraminol, phenylephrine, synephrine, octopamine, norephedrine, and ephedrine and their corresponding deoxy derivs., dopamine, epinine,  $\alpha$ -methyldopamine,  $\alpha$ -methyl m-tyramine, m-tyramine, N-methyltyramine, tyramine, (+)-amphetamine, and (+)-methamphetamine, resp. All D(-) isomers retained their ability to produce a contraction and were more active than their L(+) isomers or deoxy derivatives. L(+)-Norepinephrine and L(+)-epinephrine are essentially directly-acting and their effects were equal to those of dopamine and epinine, resp. All other L(+) isomers possess a considerable indirect component, as do their deoxy derivs., and both groups produced essentially similar effects. The results suggest that the Easson-Stedman hypothesis holds true over a wide range of substances in the catechol amine-depleted preparation but not in the untreated preparation where the dose-response curves of indirectly-acting deoxy derivs. and L(+) isomers appear to be related to their known affinity for catechol amine uptake sites. Further classification of sympathomimetic amines is carried out.

ACCESSION NUMBER: 1967:35097 CAPLUS  
 DOCUMENT NUMBER: 66:35097  
 TITLE: Steric aspects of adrenergic drugs. II. Effects of DL-isomers and deoxy derivatives on the reserpine-pretreated vas deferens

AUTHOR(S): Patil, Popat N.; LaPidus, Jules B.; Campbell, Duncan; Tye, Arthur  
 CORPORATE SOURCE: Ohio State Univ., Columbus, OH, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1967), 155(1), 13-23  
 CODEN: JPETAB; ISSN: 0022-3565

DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 120 OF 128 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB The action of D and L isomers of norepinephrine, epinephrine, cobefrin, metaraminol, phenylephrine, octopamine, synephrine, noreph. edrine, ephedrine, and pseudo ephedrine and their deoxy derivs. on the isolated rat vas deferens was studied in the light of the Easson-Stedman hypothesis that dextro isomers act like deoxy derivs. The dose-response curves and median effective dose values of L(+)-norepinephrine and L(+)-epinephrine were indeed essentially the same as those of their deoxy derivs., dopamine and epinine, resp. In all other cases, dextro isomers produced much less contraction of the vas deferens than their deoxy derivs. This indicates that in the normal vas deferens the hypothesis holds true for directly-acting L(+) isomers and their deoxy derivs., but not for indirectly-acting compds. In the latter case, dose-response curves appear to be related to the affinity of these compds. for catechol amine uptake sites. The importance of the relative configurations of the  $\beta$ -hydroxy 1 and  $\alpha$ -Me groups in relation to sympathomimetic effect is discussed.

ACCESSION NUMBER: 1967:35096 CAPLUS  
 DOCUMENT NUMBER: 66:35096  
 TITLE: Steric aspects of adrenergic drugs. I. Comparative effects of DL isomers and deoxy derivatives

AUTHOR(S): Patil, Popat N.; LaPidus, Jules B.; Tye, Arthur  
 CORPORATE SOURCE: Ohio State Univ., Columbus, OH, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1967), 155(1), 1-12  
 CODEN: JPETAB; ISSN: 0022-3565

DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 121 OF 128 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB Levels of brain amines were determined in 3 strains of chicks from hatching to 8 weeks of age, i.e., broiler strain (males), White Leghorn strain (females), and a crossbred strain of Rhode Island Reds and Barred Plymouth Rock (males). The effect of feeding excess dietary L-phenylalanine (I) on brain amines was also studied in chicks. Norepinephrine (II) and serotonin (III) levels increased in growing chicks of the broiler strain. After the 1st week of age, however, concns. of both amines showed no further increases. There was no difference in the III content among the 3 strains when compared at 4 weeks of age. However, the II content in the broiler strain was appreciably higher than those of the other strains. Feeding I had no effect on either II or dopamine level in the brain, although there was a difference in the normal level of II among the 3 strains. In the broiler strain, feeding 5% I decreased the brain III content. In the other strains, however, slight increases in III levels occurred after feeding 2 and 4% I but not at the 8%. There was no effect on brain III levels when the broiler strain was fed a basal diet for 4 weeks and then changed to a diet containing 5% I for 4 weeks, although these animals lost approx. 33% of their initial weight at 4 weeks of age. In contrast, the chicks previously fed a 5% I diet for 4 weeks and then changed to basal diet for 4 weeks gained weight rapidly and had normal or higher brain III levels.

ACCESSION NUMBER: 1967:17393 CAPLUS  
 DOCUMENT NUMBER: 66:17393  
 TITLE: Brain amines and brain weights in growing chicks. Some normal values and effects of feeding excess dietary L-phenylalanine

AUTHOR(S): Pacheldt, Gordon R.; Tamimie, Hakki S.  
 CORPORATE SOURCE: Galesburg State Res. Hosp., Galesburg, IL, USA  
 SOURCE: Biochemical Pharmacology (1966), 15(10), 1629-32  
 CODEN: BCPCAG; ISSN: 0006-2952

DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 122 OF 128 CAPLUS COPYRIGHT 2004 ACS ON STN  
 AB The turnover rates of norepinephrine were measured in rat cerebellum, hypothalamus, medulla oblongata, striatum, midbrain, hippocampus, and cerebral cortex after the animals had been given intraperitoneal injections of 200 mg. of L- $\alpha$ -methyl-p-tyrosine/kg., intraventricular injections of 1.5  $\mu$  of labeled dopamine, or after intraventricular injections of 0.15  $\mu$  of labeled DL-norepinephrine. The rate of formation of norepinephrine/g. of tissue was greater in the hypothalamus although the turnover rate is greater in the cerebellum. The 3 exptl. procedures indicated that the disposition of norepinephrine after intraventricular injections of labeled DL-norepinephrine represented metabolism of endogenous stores of norepinephrine in the brain.

ACCESSION NUMBER: 1966:432878 CAPLUS  
 DOCUMENT NUMBER: 65:32878  
 ORIGINAL REFERENCE NO.: 65:6140e-f

TITLE: Regional differences in the rate of turnover of norepinephrine in the rat brain

AUTHOR(S): Iversen, L. L.; Glowinski, J.  
 CORPORATE SOURCE: Lab. Clin. Sci., Natl. Inst. of Mental Health, Bethesda, MD  
 SOURCE: Nature (London, United Kingdom) (1966), 210(5040), 1006-8  
 CODEN: NATUAS; ISSN: 0028-0836

DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 123 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB The response of the renal vasculature to various intraarterially administered drugs was determined in rats with nephrotoxic serum nephrosis and aminonucleoside nephrosis. Norepinephrine, angiotensin, and vasopressin caused large increases in kidney perfusion pressure and (up to 100 mm.), in both nephrotic groups and their resp. controls. The renal vascular resistance was unaffected by the disease.

ACCESSION NUMBER: 1966:33562 CAPLUS  
 DOCUMENT NUMBER: 64:53562  
 ORIGINAL REFERENCE NO.: 64:10055b-c  
 TITLE: Renal vascular responses to drugs in experimental nephrosis in rats  
 AUTHOR(S): Rosenthal, Marvin E.; Baum, Thomas  
 CORPORATE SOURCE: Pharmacol.Evaluation Sect., Wyeth Labs., Inc., Radnor, PA  
 SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1965), 120(3), 689-92  
 CODEN: PSEBAA; ISSN: 0037-9727  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 124 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Antiserum injected into newborn rats for 6 or 7 days had decreased the number of cells in the superior cervical and stellate ganglia 87 and 81%, resp., when the animals were examined 2-10 months after treatment, and it also had decreased the action potentials of the adrenergic ganglia 87%. Administration of 10 mg. of the monoamine oxidase inhibitor, Catron (JB-516),/kg. increased the adrenergic content of norepinephrine in normal rats and slightly increased the content of norepinephrine in the superior cervical and stellate ganglia from antiserum-treated rats, indicating that the surviving cells in antiserum-treated rats can synthesize norepinephrine.

ACCESSION NUMBER: 1966:30066 CAPLUS  
 DOCUMENT NUMBER: 64:30066  
 ORIGINAL REFERENCE NO.: 64:5604a-b  
 TITLE: Effects of immunosympathectomy on the superior cervical ganglion and other adrenergic tissues of the rat  
 AUTHOR(S): Klingman, Gerda I.; Klingman, Jack D.  
 CORPORATE SOURCE: State Univ. of New York, Buffalo  
 SOURCE: Life Sciences (1965), 4(22), 2171-9  
 CODEN: LIFSAK; ISSN: 0024-3205  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 125 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Staining of animal brain tissues with Geigy Blue (C.I. Direct Blue 53) revealed penetration of intra-arterially injected heparin, ascorbic acid, reserpine, orphenadrine, norepinephrine, and serotonin.

ACCESSION NUMBER: 1966:14073 CAPLUS  
 DOCUMENT NUMBER: 64:14073  
 ORIGINAL REFERENCE NO.: 64:2615g-h  
 TITLE: Effect of modern (psychotropic and anticoagulant) drugs on permeability--modes of action on the blood-brain barrier  
 AUTHOR(S): Liebaltd, G.  
 CORPORATE SOURCE: Univ.-Nervenklin., Wuerzburg, Germany  
 SOURCE: Arzneimittel-Forschung (1965), 15(9), 1056-60  
 CODEN: ARZNAD; ISSN: 0004-4172  
 DOCUMENT TYPE: Journal  
 LANGUAGE: German

L16 ANSWER 126 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB Bivagotomized dogs and rabbits were pretreated with a total dose of 0.8 mg. of reserpine/kg. intramuscularly and 2-6 mg./kg. intravenously. The maximum ineffective dose of tyramine hydrochloride (I) after reserpine pretreatment was 96  $\gamma$ /kg. in dogs and 226  $\gamma$ /kg. in rabbits. In untreated dogs and rabbits the maximum ineffective dose was 15 and 42  $\gamma$ /kg., resp. Intravenous injections of 1.0 g./dog and 75 mg./kg. of L- $\alpha$ -methyldopa into reserpine-pretreated dogs and rabbits, resp., increased the pressor responses to I, reaching a maximum in 1-2 hrs.

Animals not pretreated with reserpine showed no changes in the pressor responses to I after equivalent doses of L- $\alpha$ -methyldopa. In reserpine-treated dogs and rabbits  $\alpha$ -methyldopamine in intravenous doses of 0.2 and 2 mg./kg., resp., restored the activity of I but the maximum activity occurred within the 1st hr. and 2 and 6  $\gamma$  of  $\alpha$ -methylnorepinephrine/kg. in rabbits and dogs, resp. caused immediate increases in I responses.

The pressor responses to I elicited by norepinephrine were less and of shorter duration than those of  $\alpha$ -methylnorepinephrine. The effects of methyldopa are due to its amine metabolites. Particularly indicated is  $\alpha$ -methylnorepinephrine as the mediator.

ACCESSION NUMBER: 1965:466153 CAPLUS  
 DOCUMENT NUMBER: 63:66153  
 ORIGINAL REFERENCE NO.: 63:12191h, 12192a-b  
 TITLE: Restoration of tyramine pressor responses in reserpine-treated animals by methyldopa and its amine metabolites  
 AUTHOR(S): Pettinger, William A.; Spector, Sydney; Horwitz, David; Sjoerdsma, Albert  
 CORPORATE SOURCE: Natl. Heart Inst., Bethesda, MD  
 SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1965), 118(4), 988-93  
 CODEN: PSEBAA; ISSN: 0037-9727  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English



L16 ANSWER 127 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB cf. CA 62, 13729g. The intravenous injection of amphetamine, 200  
 y/kg. at 30-min. intervals, caused tachyphylaxis after the 5th dose  
 but was not accompanied by any change in cardiac catechol amine levels.  
 The injection of tyramine, 800 y/kg. at 15-min. intervals, caused  
 tachyphylaxis after the 9th dose as well as a significant decrease in  
 catechol amine concentration as indicated by the accelerated fall in sp.  
 activity  
 of myocardial norepinephrine after injection of  
 dl-norepinephrine-7-3H. After administration of amphetamine,  
 tachyphylaxis to tyramine developed more rapidly and did not disappear  
 with repeated doses of tyramine. Amphetamine, which did not interfere  
 with the initial pressor response to tyramine nor with its release of  
 norepinephrine from the heart, seems to act by blocking the entry of  
 newly-synthesized norepinephrine into an easily released store of the  
 compound  
 ACCESSION NUMBER: 1965:457556 CAPLUS  
 DOCUMENT NUMBER: 63:57556  
 ORIGINAL REFERENCE NO.: 63:10538a-b  
 TITLE: Pressor responses to amphetamine in the spinal cat  
 and  
 its influence on tachyphylaxis to tyramine  
 AUTHOR(S): Bhagat, B.  
 CORPORATE SOURCE: Howard Univ., Washington, D.C.  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics  
 (1965), 149(2), 206-11  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L16 ANSWER 128 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN  
 AB A group of rats was injected with 0.5 ml. of  $1.9 \times 10^{-4}$  M  
 norepinephrine-7-H3 and epinephrine-1-C14. The presence of  
 tritium in the epinephrine and 3-methoxynorepinephrine zones indicates  
 that norepinephrine is converted into epinephrine in vivo. The absence  
 of  
 C14 in the norepinephrine and 3-methoxynorepinephrine zones shows that  
 epinephrine is not demethylated to norepinephrine, and the N-methylation  
 of norepinephrine to epinephrine is an irreversible process in vivo.  
 Epinephrine-H13 formed from norepinephrine-H3 is not o-methylated to the  
 same extent as originally injected epinephrine-C14.  
 ACCESSION NUMBER: 1960:119728 CAPLUS  
 DOCUMENT NUMBER: 54:119728  
 ORIGINAL REFERENCE NO.: 54:22939d-f  
 TITLE: Relative metabolic rates of norepinephrine-7-H3 and  
 epinephrine-1-C14  
 AUTHOR(S): Goldstein, M.; Friedhoff, A. J.; Sandler, G.  
 CORPORATE SOURCE: New York Univ., New York, NY  
 SOURCE: Experientia (1960), 16, 211  
 CODEN: EXPEAM; ISSN: 0014-4754  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

=> loff y

LOFF IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.

For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> logoff y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

660.05

667.72

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-166.60

-166.60

STN INTERNATIONAL LOGOFF AT 18:29:31 ON 06 DEC 2004